ABSTRACT BOEK

WETENSCHAPPELIJKE PUBLICATIES VAN AZ GROENINGE

2015
et enige trots stellen wij u de eerste editie van het abstractboek van az groeninge voor. Het kwam tot stand op initiatief van ons wetenschappelijk comité.

Hoewel wetenschappelijke activiteit traditioneel niet tot de kernopdrachten van niet-universitaire ziekenhuizen behoort, stellen we vast dat het aantal in ons ziekenhuis verrichte klinische studies ieder jaar toeneemt, dat de samenwerking met universitaire onderzoekscentra en in het bijzonder de naburige Kulak, en dus ook de meer academische studies, gestaag uitbreidt.

Klinisch wetenschappelijk werk houdt de medisch-verpleegkundige teams scherp en helpt om in tijden van concentratie van complexe en zeldzame pathologie in referentiecentra een reële expertise aan te tonen. Het werken volgens internationale kwaliteitsstandaarden, wat ons in 2016 als eerste perifere ziekenhuis in het land voor de tweede maal op rij een JCI-accreditatie opleverde, helpt daarbij.

Dit is dan ook waar wij in de komende jaren willen blijven: geneeskunde van hoog niveau, gebaseerd op wetenschappelijke evidentie, gekoppeld aan operationele excellentie en patiëntveiligheid.

DR. SERGE VANDERSCHUEREN
MEDISCH DIRECTEUR
BACKGROUND
Laparoscopic total mesorectal excision (TME) for low rectal cancer can be technically challenging. This report describes our initial experience with a hybrid laparoscopic and transanal endoscopic technique for TME in low rectal cancer.

METHODS
Between December 2012 and October 2013, we identified patients with rectal cancer < 5 cm from the anorectal junction (ARJ) who underwent laparoscopic-assisted TME with a transanal minimally invasive surgery (TAMIS) technique. A standardized stepwise approach was used in all patients. Resection specimens were examined for completeness and measurement of margins. Preoperative magnetic resonance imaging (MRI) characteristics and short-term postoperative outcomes were examined. All values are mean ± standard deviation.

RESULTS
Ten patients (8 males; median age: 60.5 (range 36-70) years) were included. On initial MRI, all tumors were T2 or T3, mean tumor height from the ARJ was 28.9 ± 12.2 mm, mean circumferential resection margin was 5.3 ± 3.1 mm, and the mean angle between the anal canal and the levator ani was 83.9° ± 9.7°. All patients had preoperative chemoradiation therapy, TME via TAMIS, and distal anastomosis. There were no intraoperative complications, anastomotic leaks, or 30-day mortality. The pathologic quality of all mesorectal specimens was excellent. The distance from the tumor to the anal verge was 19.4 ± 10.4 mm, the mean circumferential resection margin was 13.8 ± 5.1 mm, and the median lymph node harvest was 10.5 (range 5-15) nodes.

CONCLUSIONS
A combined laparoscopic and transanal approach can achieve a safe and oncologically complete TME dissection for low rectal tumors. This approach may improve clinical outcomes in these technically difficult cases, but larger prospective studies are needed.

ABSTRACT 2
Transanal endoscopic operation for benign rectal lesions and low-risk T1 carcinomas: a Belgian multicenter experience

Yoshihara E., Pottel H., Dodrey L., Vindevoghel K., D’Hoedt M., Belgian Society of Gastrointestinal Endoscopy Symposium, Belgian Week of Gastro-Enterology - February 2015 (Brussels, Belgium)

INTRODUCTION
Transanal endoscopic operation (TEO) has evolved as a new technique from transanal endoscopic microsurgery (TEM). TEM is a minimally invasive technique used for local excision of benign and selected malignant rectal lesions.

RESULTS
All patients underwent interval laparoscopic liver resection consisting of three metastasectomies, laparoscopic subsegmentectomy and laparoscopic right hemihepatec-
Laparoscopic parenchyma-preserving liver resections using the Enseal® G2 articulating sealing device – Video presentation D’Hondt M.

D’Hondt M., Yoshihara E., Vansteenkiste F., Rooy F., Devriendt D.
European Hepato-Pancreato-Biliary Association Congress - April 2015 (Manchester, UK)

BACKGROUND
Preservation of hepatic parenchyma is important in liver surgery to prevent postoperative liver failure. Furthermore, reports have been published showing a prolonged survival of minor resections compared to major hepatectomies in patients with collateral liver metastases. However, laparoscopic parenchyma-preserving liver resections can be technically challenging.

Recently a new articulating sealing device (Enseal® G2, Ethicon Endo-Surgery Inc., Cincinnati, OH) was introduced. We performed over 40 laparoscopic liver resections using this device. The aim of this video is to demonstrate the advantages of this articulating sealing device in laparoscopic liver surgery using 3 short videos.

MATERIAL & METHODS
The first patient has a solitary hepatocellular carcinoma in segment VVB. A segment VVB resection is performed using the Enseal® device. The third patient had 3 collateral liver metastases in the posterosuperior segments: one in segment 6, one in segment IVB. A segment IVB resection is performed using this device. The second patient has 2 colorectal liver metastases: one in segment 6 and one in segment IVB. The Louisville-statement defined laparoscopic resections in the posterosuperior segments in semiprone position.

CONCLUSIONS
Central venous pressure drop after blood salvage is a strong independent predictor of intraoperative blood loss during liver resection.

D’Hondt M., Clarysse M., Yoshihara E., Sergeant G., Devriendt D., Van Rooy F., Vansteenkiste F., Parmentier I.
European Hepato-Pancreato-Biliary Association Congress - April 2015 (Manchester, UK)
Belgian Surgical Week - May 2015 (Ghent, Belgium)

BACKGROUND
Although low central venous pressure (CVP) is thought to decrease blood loss during liver resection, no consistent method and safe method for obtaining this reduction of CVP has been established. Blood salvage has been proposed as a way to rapidly and consistently reduce CVP prior to parenchymal resection. Our aim was to study the impact of CVP drop (in mm Hg) after blood salvage on intraoperative blood loss during liver resection.

MATERIAL & METHODS
A consecutive series of 100 patients (M/F: 43/57, median age: 65 (23 - 91) years undergoing liver resection with blood salvage at one single non-academic teaching hospital was studied. The volume (ml) of blood salvage was set at 0.7% of body weight in kg. Primary outcome variable was intraoperative blood loss during liver resection. Multivariable logistic regression analysis was performed to identify predictors of intraoperative blood loss.

RESULTS
Fifty-seven patients underwent laparoscopic liver resection. Colorectal cancer liver metastatic disease was the indication for liver resections in 17 patients. Median (range) CVP prior to blood salvage was 8 (4 - 30) mm Hg. Median (range) volume of blood salvage was 400 (200 - 1000) ml.

After blood salvage CVP decreased to a median (range) of 3 (1.2 - 16) mm Hg, resulting in a median CVP drop of 5.5 (2 - 14) mm Hg. A Pringle-maneuver was used in thirteen patients. Median (range) intraoperative blood loss during liver resection was 165 (50 - 800) ml. Median length of hospital stay was 9 (3 - 59) days. No postoperative mortality was observed. Increasing CVP drop was significantly associated with reduced blood loss (p<0.001).

The Louisville-statement defined laparoscopic resections of posterosuperior segments (LPSS) in semiprone position.

METHODS
We reviewed a prospectively collected single-center database of all liver resections performed between August 2011 and January 2015. LLLS and LPSS were compared with respect to demographics and peroperative outcomes. Results: For the 50 patients undergoing LLLS (n=20) or LPSS (n=25).

- There were no differences in patient demographics (table) or tumour diameter (p=0.9547). There were no conversions. Pringle manoeuvre was not used in both groups. There was no difference in peroperative central venous pressure (p=0.1106). Median operative time in the LLLS group was 100 (60-260) min and 160 (95-270) min in the LPSS group (p=0.0017) with median intra-operative blood loss in the LSSS group of 500 (150-550) ml versus a larger 150 (50-700) ml (p=0.0096) for patients receiving LPSS. No patients required transfusion. Intraoperative and postoperative complication rate was similar in both groups. Mortality rate was nil in both groups. Median hospital stay was 6 days in both groups (p=0.5540).

CONCLUSIONS
LPSS in semiprone can be performed with similar clinical outcomes as a minor laparoscopic liver resection except for longer operative time and larger intraoperative blood loss without the need for transfusion.
No patients required transfusion. Intra-operative and postoperative complication rate was similar in both groups. Mortality rate was nil in both groups. Median hospital stay was 6 days in both groups (p=0.55-40).

CONCLUSIONS

LPS is in principle can be performed with similar clinical outcomes as a minor laparoscopic liver resection except for longer operative time and larger intra-operative blood loss without the need for transfusion.

ABSTRACT 7

Totally extraperitoneal laparoscopic inguinal hernia repair using a self-expanding nitinol framed hernia repair device: preliminary results of a prospective pilot study

Yoshihara E., Potthoff H., D’Hondt M.
World Conference on Abdominal Wall Hernia Surgery – April 2015 (Milan, Italy)

INTRODUCTION

Mesh shrinkage and fixation have been associated with recurrence and postoperative pain. Avoiding shrinkage and fixation could reduce postoperative pain and improve hernia recurrence rates and complications. Recently it has been shown that the self-expanding nitinol framed hernia repair device (Rebound-HRD®, MMDI, Plymouth, MN, USA) exhibits radiographic evidence of size and shape stability and intransience of position without fixation. To our knowledge no studies have been published regarding the use of this type of prosthetic for totally extraperitoneal laparoscopic inguinal hernia repair (TEP-IHR). Therefore we prospectively evaluated the use of the Rebound-HRD® mesh for TEP-IHR.

MATERIAL & METHODS

The study population comprised all patients who underwent a TEP-IHR using the Rebound-HRD®. Large mesh from April 2014 till October 2014. All operations were performed by a single surgeon (MDH) with experience of more than 80 TEP-IHR procedures. Intra- and extra-operative type and size of the hernia were evaluated according to the EHS classification. No mesh fixation was performed. Baseline characteristics for all patients were evaluated considering age, gender, BMI and American Society of Anesthesiologists score. All patients were evaluated for post-operative pain using the visual analogue scale (VAS score). Somatic, neuropathic and visceral pain were also questioned.

RESULTS

In total 36 TEP-IHR procedures were performed in 27 patients. The median operating time was 29 (range 25-35) minutes for unilateral hernia and 55 (range 40-60) minutes for bilateral hernias. The median duration of the mesh deployment was 90 (range 30-180) seconds. No peroperative complications occurred.

At the day of the operation, day 2 and day 3 the median VAS score was 3 (range 1-5), 2 (range 0-4), and 1 (range 0-3) respectively. At the time of re-evaluation at 1 week, 40% still experienced mild pain with a mean VAS score of only 1.46. Patients were completely pain-free at a median time of 5 (range 1-42) days. At 1 month only 10% of the patients experienced residual pain with a mean VAS score of 0.15. No one had pain after 3 months.

After 1 month, 1 patient felt somatic and visceral pain, 1 patient felt somatic and neuropathic pain, 1 patient mentioned only visceral pain and another patient only neuropathic pain. None of the patients could feel the sensation of a mesh in their groin.

The median length of stay was 1 day (range 1-3) day, with 78% of the patient leaving the hospital at the day of the operation. Length of stay was associated with a bilateral hernia repair (p=0.0067) and the duration of the operation (p=0.0051).

The patients were back at work after a median time of 5 (range 1-42) days. At 1 month only 10% of the patients had a wound dehiscence of a 5mm trocar wound. At a median follow-up of 3 months, no recurrences occurred.

CONCLUSIONS

With the proviso that our study population was limited in size and follow-up is relatively short, TEP-IHR using the Rebound-HRD® mesh for TEP-IHR.

ABSTRACT 8

Laparoscopic resection of rectal cancer does not result in lower low anterior resection syndrome (LARS) scores

European Society of Coloproctology Annual Meeting- September 2015 (Dublin, Ireland)
Belgian Surgical Week - May 2015 (Ghent, Belgium)

AIM

Sphincter-preserving surgery for rectal cancer is often associated with lower anterior resection syndrome (LARS). The aim of our study was to determine whether laparoscopic resection reduces LARS.

METHODS

From a prospective database 100 consecutive patients undergoing low anterior resection (TME and PME) between 01/2009 and 09/2014 were retrospectively studied. Patients were contacted after a median postoperative time of 38 months (5-45 months) to determine their LARS-score. Uni- and multivariate regression analysis was performed to identify risk factors for LARS and major LARS (3D-LARS score >42).

RESULTS

Sixty-five patients underwent neo-adjuvant chemoradiotherapy. Rectal resections consisted of TME in 74 patients. Resections were performed laparoscopically in 40 patients. An end-to-end anastomosis or J-pouch was constructed in 57 and 38 patients respectively. Postoperative anastomotic insufficiency and perioperative radiotherapy. Median LARS score was 30 (0-100). Patients undergoing laparoscopic rectal resection had significantly lower LARS scores (p=0.04).

After adjusting for age, gender, anastomotic technique, anastomotic insufficiency and perioperative radiotherapy, the laparoscopic approach was not found to be significantly associated with lower LARS-scores (adj. p=0.15) or reduced incidence of major LARS (adj. p=0.47). Radiotherapy was an independent risk factor for major LARS (p=0.04).

CONCLUSIONS

Laparoscopic resection of rectal cancer does not result in lower LARS scores. Perioperative radiotherapy is an independent risk factor for major LARS.
ABSTRACT 1
Association between urinary TIMP-2 and IGFBP7 as early biomarkers of AKI and oliguria during liver surgery: a prospective pilot study

INTRODUCTION
Patients undergoing elective liver surgery have an increased risk for developing AKI [1]. This study was intended to assess [TIMP-2][IGFBP7] and its possible association with urine output (UO) in this population. Secondly we sought to compare [TIMP-2][IGFBP7] with serum creatinine concentration (Scr).

METHODS
Prospective single center pilot performed on 12 patients undergoing elective liver surgery. Serial urine samples were analyzed for [TIMP-2][IGFBP7] measured with the Nephrocheck device (Astute Medical, San Diego, CA, USA). Serial Scr was analyzed. UO; blood losses; Mean Arterial Pressure (MAP) were recorded. Fluid management was standardized, oliguria defined as a UO <0.5mL/kg/h. \([\text{TIMP-2}] \times [\text{IGFBP7}]\) values of >0.3 identify patients at high risk and >2 at highest risk for AKI [2].

RESULTS
Males comprised 66.7%, median age was 72 years. Median surgical time was 195 min. Perioperative median MAP was 71 mmHg (IQR 66,5 mL/min/1.73m² resp). Median baseline Scr was 0.75 mg/dL (IQR 0.61;1.10), 0.74 mg/dL at ICU admission and 0.74 mg/dL at day 1 (0.64;1.04) on day 1 postoperatively. No difference in Scr and eGFR was seen between admission and 0.74 mg/dL (0.64;1.04) on day 1 postoperatively. No difference in Scr and eGFR was seen between admission and 0.74 mg/dL (0.64;1.04) on day 1 postoperatively.

ABSTRACT 2
The influence of propofol and sevoflurane on intestinal motility during laparoscopic surgery

BACKGROUND
Volatile anaesthetics have an influence on small bowel peristalsis during laparoscopic surgery. A recent study concluded that desflurane increased intestinal motility compared to sevoflurane. Hence, a desflurane-based anaesthesia protocol may reduce surgical exposure during intestinal suturing or stapling due to small bowel hyperperistalsis. The effect of propofol on intestinal motility is not well studied. We tested the hypothesis that a propofol-remifentanil group (0 vs. 6, P < 0.001).

RESULTS
The median number of peristaltic waves was lower in the propofol-remifentanil group compared to the sevoflurane-remifentanil group (0 vs. 6, P < 0.001).

CONCLUSION
Propofol-remifentanil increases intestinal motility compared to sevoflurane-remifentanil during laparoscopic gastric bypass surgery. A sevoflurane-based protocol can help to avoid disturbing peristalsis.

ABSTRACT 3
Long-term quality of life in critically ill patients with acute kidney injury treated with renal replacement therapy: a matched cohort study

INTRODUCTION
Acute kidney injury (AKI) is a common complication in intensive care unit (ICU) patients and is associated with increased morbidity and mortality. We compared long-term outcome and quality of life (QOL) in ICU patients with AKI treated with renal replacement therapy (RRT) with matched non-AKI-RRT patients.

METHODS
Over 1 year, consecutive adult ICU patients were included in a prospective cohort study. AKI-RRT patients alive at 1 year and 4 years were matched with non-AKI-RRT patients. AKI-RRT patients alive at 1 year and 4 years were matched with non-AKI-RRT survivors, but lower than in the general population.

CONCLUSION
The majority of AKI-RRT patients wanted to be readmitted to the ICU when needed, despite a higher severity of illness compared to matched non-AKI-RRT patients, and despite the fact that one quarter had persistent dialysis dependency.

ABSTRACT 4
Pneumoperitoneum does not influence spread of local anesthetics in midaxillary approach transverse abdominis plane block: a descriptive cadaver study

BACKGROUND AND OBJECTIVES
The transversus abdominis plane (TAP) block can be used as part of a multimodal analgesia protocol after abdominal surgery. This study investigated whether a pneumoperitoneum during abdominal surgery influences the spread of local anesthetics.

METHODS
Nine fresh frozen cadavers were used for the study. Using an ultrasound-guided midaxillary technique, a unilateral TAP block was performed during pneumoperitoneum during 1 hour. Pneumoperitoneum does not influence spread of local anesthetics.

RESULTS
No difference in spread of local anesthetics was seen between the study periods. The planned site of the jejunostomy. Statistical analysis was performed using Wilcoxon two-sample test.

RESULTS
After obtaining written informed consent 50 patients were included. Groups were similar for demographic variables, and depth of anesthesia during the observations. The median number of peristaltic waves was lower in the sevoflurane-remifentanil group compared to the propofol-remifentanil group (0 vs. 6, P < 0.001).

CONCLUSION
Propofol-remifentanil increases intestinal motility compared to sevoflurane-remifentanil during laparoscopic gastric bypass surgery. A sevoflurane-based protocol can help to avoid disturbing peristalsis.

ABSTRACT 5
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ABSTRACT 4
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The transversus abdominis plane (TAP) block can be used as part of a multimodal analgesia protocol after abdominal surgery. This study investigated whether a pneumoperitoneum during abdominal surgery influences the spread of local anesthetics.

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Nine fresh frozen cadavers were used for the study. Using an ultrasound-guided midaxillary technique, a unilateral TAP block was used as part of a multimodal analgesia protocol after abdominal surgery. This study investigated whether a pneumoperitoneum during abdominal surgery influences the spread of local anesthetics.
RESULTS

In none of the specimens did the dye reach the posterior origin of the transverse abdominal muscle. There was no statistically significant difference in the number of stained nerves and spread of the dye in the insufficiently side compared with the normally sized side. In 4 of 9 cadavers, we found a variant course of a nerve preventing staining of that nerve.

CONCLUSIONS

The stretch of the abdominal wall caused by the insufflation of the abdomen does not influence the spread of dye in the abdominal wall. Because of the absence of posterior spread, regardless of the timing of a midaxillary ultrasound-guided approach, we believe that a posterior approach should be chosen if posterior spread is desired.

ABSTRACT 5

A randomised controlled trial of intravenous dexames-thasone combined with interscalene brachial plexus blockade for shoulder surgery


We recruited patients scheduled for shoulder rotator cuff repair or subacromial decompression under general anaesthesia and interscalene brachial plexus blockade (30 ml ropivacaine 0.5%). We allocated 240 participants into four groups of 60 that were given pre-operative saline 0.9% or dexamethasone 1.25 mg, 2.5 mg or 10 mg intravenously. We recorded outcomes for 48 h. The median (IQR) [range] time to first postoperative analgesic request was 12.2 (11.0-14.1 [1.8–48.3]) h, which was extended by intravenous dexamethasone 2.5 mg and 10 mg to 17.4 (14.9-21.5 [7.2-48.1]) h, p = 0.0001, and 20.1 (17.2-24.3 [3.1–48.6]) h, p = 0.0001, respectively, but not by dexamethasone 1.25 mg, 14.0 (12.1-17.7 [2.1–48.6]) h, p = 0.0001.

CONCLUSIONS

We performed a study to assess the efficacy of the longitudinal suprainguinal fascia iliaca compartment block for total hip arthroplasty


Aims

Total hip arthroplasty (THA) is painful surgery. Posterior lumbar plexus blocks and more distal nerve blocks (eg femoral nerve block or fascia iliaca compartment block) have been described for postoperative analgesia. This is a two centre, double blind, randomized controlled trial where we compared the opioid consumption of patients with and without a longitudinal suprainguinal fascia iliaca compartment block (FICB).

METHOD

A double centre observational trial was performed in patients undergoing total hip arthroplasty. After induction of anaesthesia, we performed an ultrasound-guided FICB according to the approach described by Hebbard. This ultrasound-guided supra-inguinal technique allows an easy identification of the fascia iliaca compartment. After correct positioning of the needle 40 mL of ropivacaine 0.5% was injected. One hour postoperatively, we evaluated the sensory block and motor block in the different nerve territories as described by Neal.

RESULTS

After ethical committee approval and obtaining written informed consent, 43 patients were included. Table 1 presents the results for sensory and motor blockade for the different nerves in 32 of 43 patients (75%) of the patients all three nerves were blocked.

CONCLUSIONS

The longitudinal suprainguinal FICB successfully blocks the femoral and obturator nerve, as well as the lateral cutaneous nerve. The longitudinal supra-inguinal FICB seems to be a successful and reliable approach.
METHOD
After Institutional Review Board approval and written informed consent, patients were included in a double-blinded, placebo-controlled study and were randomly allocated to one of the two research groups. One group received a FICB (Group FICB) with 40mL ropivacaine 0.5%, compared to a control group (Group C) without FICB. All patients received paracetamol, NSAIDs and a patient controlled intravenous analgesia system (PCA) with morphine for postoperative pain relief. Baseline demographics and results were analyzed using Mann-Whitney U test. As primary endpoint was postoperative morphine consumption at 24 and 48 hours.

RESULTS
We included 78 patients (Group FICB = 38, Group C = 40). There were 49 women and 29 men. Mean age was 60 and 65 years for Group FICB and Group C, respectively (p=0.03). BMI was comparable for both groups. The mean morphine consumption at 24 and 48 hours was 8.8 and 10.9 mg for Group FICB compared to 16.9 and 20.8 mg for Group C (at 24h p=0.001, at 48h p=0.001).

CONCLUSIONS
A longitudinal supra-inguinal fascia iliaca compartment block (FICB) for postoperative pain relief after an anterior total hip replacement significantly decreases morphine consumption at 24 and 48 hours.

METHOD
After Institutional Review Board approval and written informed consent was obtained in 10 patients planned for total hip arthroplasty. An ultrasound-guided FICB was performed using 40 mL ropivacaine 0.5%. Arterial blood samples were taken at different time points and total serum ropivacaine levels were determined using a Liquid Chromatography-Mass Spectrometry method. All patients were monitored for neurological and cardiac symptoms of local anesthetic systemic toxicity. Values are presented as means (range).

RESULTS
Figure 1 presents the pattern of total arterial serum levels over time for all patients and the mean values. The mean (range) peak arterial serum level (Cmax) was 1.41 (0.8–1.6) mg/L. Time to reach Cmax was 55 (15–90) minutes after performance of the FICB. In all patients, the Cmax was lower than the maximum tolerated concentrations (3.4–5.3 mg/L) described in previous studies. None of the patients experienced neurological or cardiac symptoms of local anesthetic systemic toxicity.

CONCLUSIONS
Total serum ropivacaine levels remain under the toxic thresholds after a FICB with 40 mL ropivacaine 0.5%. Further research is necessary to determine free plasma ropivacaine levels.

ABSTRACT 1
Deprescribing psychoactive medication for geriatric patients in a multidisciplinary way.

Desmet S., Kindt D., Verhaeghe A., Verhelle K.
European Association of Hospital Pharmacists Annual Congress - March 2015 (Hamburg, Germany)

BACKGROUND
A lot of studies emphasize the incidence of serious harms caused by polymedication in elderly patients. Especially the use of benzodiazepines and/or combination with other psychoactive medication increase the risk for confusion, falls, cognitive impairment, and other adverse drug events.

OBJECTIVE
Guarding the safety and quality of life for geriatric patients with polymedication by reducing the use of psychoactive medication in a multidisciplinary way with the clinical pharmacist, geriatrician, general practitioner and home pharmacist.

METHODS
During a test of five weeks, patients were screened. The inclusion criteria were the presence of a contra-indication for benzodiazepines, a dose equivalent to 20mg diazepam or a pharmacodynamic synergistic interaction (antidepressant, antipsychotics, anticholinergics, sedative antihistaminics and opioids). The clinical pharmacist informed the patient about the impact of benzodiazepines. If the patient agreed to reduce the psychoactive medication, the geriatrician and general practitioner were contacted to decide which medication to reduce and to confirm the reduction schedule.

RESULTS
In the test 30 patients met the inclusion criteria. 6 were not approachable, for 4 patients the psychoactive medication was already stopped in the hospital. 70% of the patients informed agreed to reduce their psychoactive medication. 10% was excluded by the geriatrician, for 15% reduction was suggested via the discharge letter. The general practitioner always supported the effectuation of the reduction.

CONCLUSIONS
Deprescribing psychoactive medication for elderly people can successfully be implemented by the development of a multidisciplinary workflow (clinical pharmacist – specialist – general practitioner – home pharmacist) and by providing some practical tools. Our goal of patient safety could be achieved and led to satisfaction of patients and caregivers.
ABSTRACT 1

Cardiac ischaemia following BIB®-placement


The saline-filled Bioenterics Intragastric Balloon (BIB®) has been considered an effective treatment for obesity in combination with dietary and behavioural measures. By occupying gastric space the sensation of satiety is enhanced. A 22-year-old female presented at the emergency ward with angina since 4 hours, shortly after BIB®-placement. The electrocardiogram showed sinus tachycardia with ST-elevation in a VR and widespread horizontal ST-depression. High sensitive troponin was slightly elevated. Based on history, clinical and biochemical findings, coronary artery disease, per(ny)carditis or non-cardiac causes were very unlikely. Immediate resolution of symptoms and ECG signs was obtained after removal of the BIB®. Several mechanisms for BIB®-placement causing cardiac ischaemia were postulated. First, direct compression from the balloon on the right atrium or ventricle could have caused decreased left ventricular filling with as a result low cardiac output and coronary hypoperfusion. However, in our case no signs of cardiac compression could be seen on CT thorax and abdomen nor on echocardiography. Secondly, hyperventilation as a response to the abdominal pain, could have caused an alkalotic state that triggers intracellular influx of calcium ions, thereby provoking coronary vasospasm and myocardial ischaemia. Unfortunately, no arterial blood gasses were measured in our patient. Finally, as demonstrated in both anatomical and physiological studies in both animals and humans, linked angina and a cardio-oesophageal reflex could have been triggered by mechanical stimulation of the oesophagus and stomach. To our knowledge this is the first case of myocardial ischaemia related to BIB®-placement, thereby illustrating its possibly dangerous complications.

ABSTRACT 2

Mutations in a TGF-β ligand, TGFβ3, cause syndromic aortic aneurysms and dissections


BACKGROUND

Aneurysms affecting the aorta are a common condition associated with high mortality as a result of aortic dissection or rupture. Investigations of the pathogenic mechanisms involved in syndromic types of thoracic aortic aneurysms, such as Marfan and Loeys-Dietz syndromes, have revealed an important contribution of disturbed transforming growth factor (TGF-β) signaling.

OBJECTIVES

This study sought to discover a novel gene causing syndromic aortic aneurysms in order to unravel the underlying pathogenesis.

METHODS

We combined genome-wide linkage analysis, exome sequencing, and candidate gene Sanger sequencing in a total of 470 index cases with thoracic aortic aneurysms. Extensive cardiological examination, including physical examination, electrocardiography, and transthoracic echocardiography was performed. In adults, imaging of the entire aorta using computed tomography or magnetic resonance imaging was done.

RESULTS

Here, we report on 43 patients from 11 families with syndromic presentations of aortic aneurysms caused by TGFβ3 mutations. We demonstrate that TGFβ3 mutations are associated with significant cardiovascular involvement, including thoracic/aortic aneurysms and dissection, and mitral valve disease. Other systemic features overlap clinically with Loeys-Dietz, Shprintzen-Goldberg, and Marfan syndromes, including cleft palate, bifid uvula, skeletal overgrowth, cervical spine instability and clubfoot deformity. In line with previous odds in aortic wall tissues of patients with mutations in effectors of TGF-β signaling (TGFBR1/2, SMAD3, SMAD1, SMAD2, SMAD3), we confirm a paradoxical up-regulation of both canonical and noncanonical TGF-β signaling in association with up-regulation of the expression of TGF-β ligands.

CONCLUSIONS

Our findings emphasize the broad clinical variability associated with TGFβ3 mutations and highlight the importance of early recognition of the disease because of high cardiovascular risk.

ABSTRACT 3

Does sex affect anticoagulant use for stroke prevention in nonvalvular atrial fibrillation? The prospective global anticoagulant registry in the FIELD-Atrial Fibrillation


BACKGROUND

Among patients with atrial fibrillation (AF), women are at higher risk of stroke than men. Using prospective cohort data from a large global population of patients with nonvalvular AF, we sought to identify any differences in the use of anticoagulants for stroke prevention in women and men.

METHODS AND RESULTS

This was a prospective multicenter observational registry with 858 randomly selected sites in 30 countries. A total of 17 184 patients with newly diagnosed ≤6 weeks nonvalvular AF and ≥1 additional investigator-defined stroke risk factor(s) were recruited (March 2010 to June 2013). The main outcome measure was the use of anticoagulants (vitamin K antagonists, factor Xa inhibitors, and direct thrombin inhibitors) for stroke prevention at AF diagnosis. Of 17 184 patients enrolled, 43.8% were women. Anticoagulant use was not different overall (60.9% of men versus 60.8% of women) and in patients with a CHADS2 score of ≥1 in men versus ≥2 in women, 35.4% of men and 38.4% of women received an anticoagulant. More women than men were at moderate-to- high risk of stroke (CHA2DS2-VASc score ≥2), 35.4% of men and 38.4% of women with nonvalvular AF and ≥1 additional investigator-defined stroke risk factor(s) were recruited (March 2010 to June 2013). The main outcome measure was the use of anticoagulants (vitamin K antagonists, factor Xa inhibitors, and direct thrombin inhibitors) for stroke prevention at AF diagnosis. Of 17 184 patients enrolled, 43.8% were women. Anticoagulant use was not different overall (60.9% of men versus 60.8% of women) and in patients with a CHADS2 score ≥2 versus men, 1.00; 95% confidence interval, 0.92-1.09). In patients at low risk (CHA2DS2-VASc of 0 in men and 1 in women), 41.8% of men and 41.1% of women received an anticoagulant. In patients at high risk (CHA2DS2-VASc ≥2), 35.4% of men and 38.4% of women did not receive an anticoagulant.

CONCLUSIONS

These contemporary global data show that anticoagulant use for stroke prevention is no different in men and women with nonvalvular AF. Thromboprophylaxis was, however, suboptimal in substantial proportions of men and women, with underuse in those at moderate-to-high risk of stroke and overuse in those at low risk.
ABSTRACT 1

Outcome of 12 antenatally diagnosed fetal arachnoid cysts: case series and review of the literature

De Keersmaecker B., Ramackers P., Claus F., Witters I., Ortibus E., Naulaers G., Van Caenbergh F., De Catte L. World Congress in Fetal Medicine – June 2015 (Crete, Greece)

OBJECTIVES

To investigate the natural history, associated abnormalities, pregnancy outcome and postnatal follow-up of all cases of antenatally diagnosed arachnoid cysts, of the last 30 years, were evaluated.

RESULTS

Fetal arachnoid cysts were diagnosed in 12 fetuses, 9 were females. The mean gestational age at diagnosis was 28 1/7 (range 19 1/7-34 2/7 weeks). A total of 9 cases were reported in the literature. In 2 cases of isolated subependymal cysts on ultrasound and MRI in the postnatal period.

CONCLUSIONS

The majority of arachnoid cysts in this series are of benign origin and remain stable. Based on the current series and the review of the literature, in the absence of other associated anomalies and when the cyst is not normal, the postnatal overall and neurological outcome is favorable.

ABSTRACT 2

Subependymal cysts in the fetal brain: prenatal diagnosis of 9 cases

De Keersmaecker B., Jansen K., Naulaers G., De Catte L. World Congress in Fetal Medicine – June 2015 (Crete, Greece)

OBJECTIVE

Subependymal cysts are usually located in the wall of the caudate nucleus or in the caudato-thalamic groove. They are found in up to 5% of all neonates. When isolated, they regress spontaneously and their prognosis is good.

RESULTS

In 2 cases of isolated subependymal cysts on ultrasound and MRI. In one patient 2 small cysts were diagnosed at 25 weeks of gestation. In the other one a single cyst was found at 33 weeks. In the remaining 7 cases, 3 patients had a primary CMV seroconversion in the first trimester with a positive amniotic fluid PCR in all cases. In 2/3 patients the fetal MRI confirmed the ultrasound diagnosis and a termination of pregnancy (TOP) was performed at 23 and 30 weeks respectively. The remaining patient declined MRI and this pregnancy is still ongoing. In 1 patient a huge cyst (47x38x49 mm) was found at 36 weeks of pregnancy. Postnatally the diagnosis of plexus papilloma grade 2 was made. This child underwent surgery and chemotherapy and is doing well at the age of 6 years. The 2 patients with multiple subependymal cysts were associated with progressive ventriculomegaly. MRI confirmed the ultrasound diagnosis of 5 postnatally and metabolic investigation is still ongoing. The other baby died at the age of 8 months. The diagnosis of respiratory chain deficiency was made due to a mutation in the mitochondrial DNA (ND1). Finally, multiple subependymal cysts were found at 26 weeks in a dioxoronic diaminonic twin pregnancy. The infectious etiology was negative and there were no associated anomalies. A selective feticide was carried out at 31 weeks and investigation revealed a molybdenum cofactor deficiency / sulphate oxidase deficiency.

CONCLUSIONS

Although already described in the first trimester of pregnancy, our series of subependymal cysts were detected in the second and third trimester. Fetal MRI may be of help to rule out other brain abnormalities and TORCH screening to rule out infectious origin. Subependymal cysts with associated anomalies often result in adverse outcome.

PRESENTATIES CONGRESSEN

ABSTRACT 1

Subependymal cysts in the fetal brain: prenatal diagnosis of 9 cases

De Keersmaecker B., Jansen K., Naulaers G. & De Catte L. World Congress in Fetal Medicine – June 2015 (Crete, Greece)

OBJECTIVE

Subependymal cysts are usually located in the wall of the caudate nucleus or in the caudato-thalamic groove. They are found in up to 5% of all neonates. When isolated, they regress spontaneously and their prognosis is good.

RESULTS

Two neonates underwent endoscopic fenestration of the arachnoid cyst in the first week of life with no additional intervention in childhood. All but one (10/11) had a favorable postnatal outcome. This child suffered from visual impairment at autism was diagnosed at the age of 5. One child had a surgical correction of strabismus later in childhood. In one child the infratentorial arachnoid cyst regressed spontaneously on ultrasound and MRI and the postnatal period.

CONCLUSIONS

The majority of arachnoid cysts in this series are of benign origin and remain stable. Based on the current series and the review of the literature, in the absence of other associated anomalies and when the cyst is not normal, the postnatal overall and neurological outcome is favorable. Large supratentorial arachnoid cysts however, may cause visual impairment and endocrinological disturbances. Rarely associated cerebral or cerebellar malformations are present. Modern postnatal management of supratentorial arachnoid cyst consists of endoscopic cyssectomy.

ABSTRACT 2

Outcome of antenatally diagnosed intracranial hemorrhage: case series of 19 patients

De Keersmaecker B., Jansen K., Naulaers G. & De Catte L. World Congress in Fetal Medicine – June 2015 (Crete, Greece)

OBJECTIVE

Factors predisposing to in utero ICH (intracranial hemorrhage) include a variety of conditions, mostly maternal trauma and fetal coagulation disorders. In many cases, the etiology is not revealed. The incidence is estimated at 1 in 10 000 pregnancies. The objective of this study was to determine the sonographic criteria for the diagnosis of fetal ICH, the role of MRI and the clinical implications and outcomes of this condition in our case series of 19 patients.

METHODS

We retrospectively reviewed all of our cases of ICH diagnosed antenatally from 2006 to 2015. All patients were offered MRI. The cases were categorized as extracerebral (subdural) and intraventricular hemorrhage (IVH). IVH was subdivided in supratentorial and posterior fossa hemorrhage. Intraventricular hemorrhages were categorized following the classification commonly used in neonates.

RESULTS

Of the 15 cases of fetal ICH, there were 3 subdural bleedings and 2 hemorrhages in the posterior fossa. Of the 14 intracerebral hemorrhages, 3 cases were of Grade 1, 1 case of Grade II, 4 cases of Grade III and 6 cases of Grade IV. Diagnosis was made at a mean GA of 29 5/7 weeks (SD: 5, 1 days). In 12/19 cases ventriculomegaly was the first and most common ultrasound finding. Two Grade I bleedings were associated with TTTS in 2 MCDA twin pregnancies. A third case was associated with a second trimester CMV infection. All these children are doing well postnatally. In the fetus with Grade II intraventricular hemorrhage, it initially presented with a thrombus in the third ventricle, progressing into ventriculomegaly subsequently. A vascular malformation in the choroid plexus was also diagnosed. In the four cases of Grade III bleeding with severe bilateral ventriculomegaly (<15 mm) no etiology was found. All but one child shows neurodevelopmental impairment. Of the 6 Grade IV cases, all but one had a termination of pregnancy, the child died on day 9 postnatally. In our 3 cases of subdural bleeding, 2 underwent TOP and 1 child died day 5 postnatally. In 2 of these cases a coagulation disorder was found. (C00 (SPF 87) and the COLL / ADP 66s; Factor V gen mutations). The 2 hemorrhages in the posterior fossa were due to Parvovirus B19 infection. One child had bleeding and necrosis of the cerebellar hemisphere and a TOP was accepted. The other is doing well. A plausible cause for the hemorrhage was found in 16/19 cases. In 15/19 fetuses fetal MRI was performed. In addition to confirming the diagnosis it also added extra information e.g. the extent of the bleeding and the parenchymal involvement.
CONCLUSIONS
Diagnostic of IVH is usually made late in second/third trimester. The most common ultrasound finding in our series was ventriculomegaly. MRI allows evaluation of the entire cerebral parenchyma although it adds little additional information compared to the prenatal ultrasound. No losses were reported in IVH grade I or II. All subdural hematoma in our series were due to coagulation disorders.

ABSTRACT 3
Real-time virtual sonography using MRI and ultrasound fusion imaging in the evaluation of CNS anomalies
De Kaersnaecker B., Jansen K., Naulaers G., De Catte L.
World Congress in Fetal Medicine – June 2015 (Crete, Greece)

OBJECTIVE
Over the last years prenatal ultrasound has experienced the benefits of high resolution probes and the use of transvaginal ultrasonic to facilitate the difficult diagnosis of neural centers in brain anomalies. In addition fetal MRI has become a part of a complementary tool in establishing and fine tuning the diagnosis and prognosis. Both techniques deliver their maximal potential in the hands of clinical experts. Unfortunately the experts for fetal ultrasound and fetus MRI are most of the time not the same. The combination of ultrasound and MRI could provide the benefits from both techniques. The MRI and ultrasound fusion technology has been introduced into medicine and has been successful to diagnosis and treatment of tumors. The technology allows the combination of MRI and ultrasound images. Only one paper addressed the potential of this technique in prenatal diagnosis. AIM The aim of this study is to evaluate the additional value of real-time virtual sonography in central nervous system anomalies and to look for the gestational age on the feasibility. Does the fusion imaging technique, performed by a fetal medicine specialist, provide more information than the images of the prenatal ultrasound and MRI could be fused into one image? RESULTS
In our Fetal Medicine Unit, we performed during a 4 month period (April 2014–August 2014) 14 MRI-US fusions to evaluate the fetal brain in cases of suspected central nervous system malformation. 14 patients with a CNS anomaly were offered to undergo a fusion imaging. The fetal MRI was loaded into the DICOM (Digital Imaging Communications in Medicine) system and combined scanning was started within 30/60 minutes after the MRI. The images were synchronized in the same plane using 3 anatomical reference points. The feasibility of real-time fusion was evaluated compared to B-Mode Ultrasound and MRI.

RESULTS
5 patients were referred for CMV virenconversion in the first trimester of pregnancy. 2 patients were referred for ventriculomegaly and one for discordant ventricles. 2 patients with spina bifida and one patient with meningo-myelocele were included. One patient had a subdural bleeding while another patient had IVH grade 1. In the last patient a subependymal cyst was diagnosed. Real time virtual sonography was technically possible in all patients. Data registration, matching and fusion imaging were performed in less than 30 minutes after the MRI and was possible from 26 weeks onwards. In the ability to identify and to assess CMV related abnormalities we did not find additional information due to the fusion technique. In one patient polymericripsy was not depicted on ultrasound but seen on fetal MRI. Fusion was not conclusive in this case. In another CMV patient a cyst was suspected in the posterior horn and picked up by MRI. Fusion only confirmed the presence of this cyst. In the 2 cases of intraventricular hemorrhage the fetal MRI confirmed the ultrasound report. Fusion did not demonstrate parenchymal compression or cortical lesions missed by US/MRI. In the patient with the subependymal cyst, ultrasonography was able to visualize the septa in the cyst while MRI/fusion was less accurate to identify these small septa. In the cases of spina bifida, meningo-myelocele and ventriculomegaly the images of the prenatal ultrasound and MRI could be matched but no additional information was given by the real time sonography. Fetal MRI confirmed the exact location and size of the spinal lesion previously diagnosed by ultrasound. In the 3 cases of ventriculomegaly the US and MRI images could be merged but no additional information of the fetal brain was found.

CONCLUSIONS
Fusion imaging is feasible in the assessment of CNS affected fetuses from 26 weeks onwards. Fusion of ultrasound and MRI images does not show anatomical details that would not be seen by US or MRI alone. However data integration of both modalities could improve the multi-disciplinary prognostic appraisal as well as the prenatal counseling.

ABSTRACT 4
The occurrence of thrombosis in inflammatory bowel disease is reflected in the clot lysis profile
Inflamm Bowel Dis. 2015 Nov;21(11):2540-2548.

BACKGROUND
The occurrence of thromboembolic events (TE) is an important extra-intestinal manifestation in patients with inflammatory bowel disease (IBD). The aim of this study was to compare fibrinolysis and clot lysis parameters between (1) patients with IBD and healthy controls and (2) patients with IBD with TE (IBD + TE) and without TE (IBD - TE).

METHODS
One hundred thirteen healthy controls and 202 patients with IBD, of which 84 patients with IBD + TE and 118 patients with IBD - TE, were included in this case-control study. Three clot lysis parameters (area under the curve, 50% clot lysis time, and amplitude) were determined using a clot lysis assay. Plasminogen activator inhibitor 1 (PAI-1) and thrombin activatable fibrinolysis inhibitor (TAFI) concentrations were determined by enzyme-linked immunosorbent assay.

RESULTS
50% clot lysis time and area under the curve, were significantly associated with the presence of IBD (all P < 0.05). The median time between TE and plasma collection was 5.0 (1.8–11.0) years. Comparing IBD + TE versus IBD - TE, active to total PAI-1-ratio (0.36 (0.24–0.61) versus 0.24 (0.13–0.40); area under the curve (31 (24–49) versus 22 (13–31)); 50% clot lysis time (110 (64–132) versus 95 (70–126) minutes), and amplitude (0.205 (0.022–0.436) versus 0.241 (0.169–0.306) were significantly higher in IBD + TE (all P < 0.05) and remained higher after adjustment for age, gender, C-reactive protein, type of disease, presence of comorbidities, and disease activity.

ARTIKELS

ABSTRACT 5
The Belgian experience with triple therapy with beclo- previr and telaprevir in genotype 1 infected patients who inject drugs

No data have been reported yet on treatment outcome in patients who inject drugs (PWID) infected with hepatitis C virus treated with becovpre or telaprevir in combination with peginterferon (Peg IFN) and ribavirin (RBV). Additionally, there are concerns about the safety of becovpre or telaprevir, as some subgroups of patients with hepatitis C (HCV). In a cohort of HCV patients infected with genotype 1, treatment of patients infected due to IV drug use was analyzed and compared with patients who have no history of substance use. The study population consisted of 179 patients: 78 PWID and 101 controls treated with becovpre (n = 79) or telaprevir (n = 100) additional to Peg IFN and RBV; 53 (30%) had advanced disease (F3, F4) and 79 (44%) had an antiviral therapy previously. There were no significant differences in the baseline characteristics between both groups, except that PWID patients were more frequently infected by genotypic a (47%) and were predominantly male. Psychiatric complaints during follow-up occurred more frequently in the PWID patients: 24% versus 11% (P = .02). Treatment failure for other reasons than absence of viral response was 70% and 64% in PWID and non-PWID respectively. The sustained viral response (SVR) rates were similar in both groups (71% in PWID vs 72% in non-PWID), with a non-inferiority test with 5%-margin there is a difference of -1% (95% CI [-15%, 11%]) and P = 0.30. There are no reasons to exclude PWID from treatment with becovpre, telaprevir and novel antiviral therapies.

CENTRUM
INWENDIGE ZIEKTEKEN / GASTRO-ENTEROLOGIE

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FIBROSEN ZIEKTEKEN / GASTRO-ENTEROLOGIE
ABSTRACT

Selecting IBD patients who will benefit from thromboprophylaxis through a risk assessment that includes clot lysis parameters and clinical assessment


Unitend European Gastroenterology-Week - October 2015 (Barcelona, Spain)

BACKGROUND

Patients with inflammatory bowel disease (IBD) have a higher risk of developing thrombo-embolic events (TE) compared to the healthy population. TE has a substantial impact on mortality in IBD and TE prevention requires improved awareness and management.

Aim To describe the clinical characteristics of IBD patients with a history of TE and to compare markers of clot lysis between (1) IBD patients and healthy controls (HC) and (2) IBD patients with (IBD-TE) and without a history of TE (IBD-TE).

METHODS

84 IBD patients in whom a TE occurred (between January 1987 and March 2014) after the diagnosis of IBD, seen at discharge. To date, IBD patients with a high risk for TE are given thromboprophylaxis. However, for the patients with low to moderate risk for TE it is less clear who will benefit from prophylactic therapy. Therefore, we propose to perform a risk assessment in which clot lysis parameters and IBD specific risk factors for TE are combined to identify the patients who can benefit from prophylactic therapy with low molecular weight heparins.

CONCLUSIONS

This study reveals that IBD patients have an altered clot lysis profile compared to healthy controls. In addition, the clot lysis parameters differ significantly between IBD patients with and without a history of TE. Of the IBD patients with a history of TE, 36% received steroids at time of TE and 37% underwent recent surgery of whom only a minority received thromboprophylaxis at hospital discharge. To date, IBD patients with a high risk for TE are given thromboprophylaxis. However, for the patients with low to moderate risk for TE it is less clear who will benefit from prophylactic therapy. Therefore, we propose to perform a risk assessment in which clot lysis parameters and IBD specific risk factors for TE are combined to identify the patients who can benefit from prophylactic therapy with low molecular weight heparins.

ABSTRACT 2

Tuberculosis: the past and the future.

De Waele L., Lagae L., Meckhi D.


Renal lesions represent the second most important cause of morbidity and mortality in patients with tuberculous sclerosis complex (TSC). Recent advances in the understanding of the pathophysiology of TSC have led to the exploration of new potential therapeutic targets. Clinical trials with mammalian target of rapamycin (mTOR) inhibitors demonstrated promising results for several indications such as renal angiomylipoma, subependymal giant cell astrocytoma, lymphangioleiomyomatosis and facial angiofibromas. Recently, the diagnostic criteria, and the recommendations for surveillance and management of TSC patients have been updated. This review focuses on these novel recommendations and highlights the need for multidisciplinary follow-up of this multi-systemic disease.

ARTIKELS

ABSTRACT 1

Charcot-Marie-Tooth: are you testing for proteinuria?

De Rechter S., De Waele L., Lievchenko E., Meckhi D.


Charcot-Marie-Tooth disease (CMT) is a clinically and genetically heterogeneous group of inherited disorders affecting motor and sensory nerves of the peripheral nervous system. CMT has been reported to be associated with renal diseases, most frequently focal segmental glomerulosclerosis (FSGS). However, it has been unclear whether these two pathological processes involving the kidneys and the kidneys, represent one disorder or separate entities. Several reports have now shown a high prevalence of mutations (2%) in the gene inverted formin (INF2) in patients with CMT-associated glomerulopathy, suggesting that these mutations are a common cause of the dual phenotype. For this reason, we strongly suggest to analyse urine samples for proteinuria in CMT patients, in order to detect patients with this renal-neurologic phenotype in an early stage, and to perform genetic testing for INF2 mutations.

ARTIKELS

ABSTRACT 3

Characterization of human disease phenotypes associated with mutations in TREV1, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, ADAR and IFIH1


Acardi-Goutières syndrome is an inflammatory disease occurring due to mutations in any of TREV1, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, ADAR or IFIH1. We report on 374 patients from 299 families with mutations in these seven genes. Most patients conformed to one of two fairly stereotyped clinical profiles, either exhibiting an in utero disease-onset (74 patients; 22.8% of all patients where data were available), or a post-natal presentation, usually within the first year of life (223 patients; 66.6%), characterized by a sub-acute encephalopathy and a loss of previously
ABSTRACT 1

Renal function in children and adolescents with Duchenne Muscular Dystrophy


OBJECTIVE

To describe the long-term renal outcome in a large cohort of TSC patients. Our study describes the long-term renal outcome in a large cohort of TSC patients. The Everolimus For Fast Expanded aCcess in TSC SEGA retrospective study confirmed the acceptability safety profile of everolimus in patients with TSC in a real world setting. Results further support the efficacy of everolimus in real life setting. In this phase 3b, multicenter, expanded access study, patients ≥3 years of age with a definite diagnosis of TSC, with at least one TSC lesion identified by MRI or CT scan received once daily everolimus, the dose of which was adjusted to attain a trough level of 515 ng/ml. Safety assessments included collecting adverse events (AEs) and serious adverse events (SAEs), with their severity and relationship to everolimus. Efficacy evaluation, which was the secondary objective, was based on the best overall response at the end of the study. Overall, 100 of 120 (83.3%) patients completed the study. Median age of patients was 11 years (range 2-14). Median daily dose of everolimus was 5.82 mg (range 2.0-11.8); median duration of exposure was 56.5 weeks (range 0-130). Overall, AEs were reported in 89 (74.2%) patients; the most common AEs were gynecomastia (18%, 15%), pyrexia (18%, 15%), bronchitis (11%, 9.2%), and asthenia (10.8%). Grade 3 and 4 AEs were reported in 35 (29.2%) and 22 (18.3%) patients, respectively. The most frequent grade 3 AE was stomatitis (4, 3.3%). A total of 62 (51.7%) patients had suspected drug-related AEs, of which 15 (12.5%) were of grade 3 or 4 in 8 (6.7%) patients. AEs caused drug discontinuation. A total of 81 (67.5%) patients had a partial response, 35 (29.2%) patients had a stable disease, and 1 (0.8%) patient had progressive disease. Response was unknown in 2 (1.7%) patients. This study confirms the acceptable safety profile of everolimus in patients with TSC associated with TSC in a real world setting. Results further support the efficacy of everolimus in the treatment of TSC associated with TSC.

ABSTRACT 2

Everolimus for patients with subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC): results from an expanded access study

De Waal L., Vogels N., Pappas K., Parekh D., O’Connor D., Zaias N., Vermeersch B., Mekahli D., Jansen A.

European Paediatric Neurology Society Congress - May 2015 (Vienna, Austria)

The Everolimus For Fast Expanded access in TSC SEGA (EFFECTS) study was designed to provide early access to everolimus for patients with subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC) and to further assess the safety and efficacy of everolimus in real life setting. In this phase 3b, multicenter, expanded access study, patients ≥3 years of age with a definite diagnosis of TSC, with at least one SEGA lesion identified by MRI or CT scan received once daily everolimus, the dose of which was adjusted to attain a trough level of 515 ng/ml. Safety assessments included collecting adverse events (AEs) and serious adverse events (SAEs), with their severity and relationship to everolimus. Efficacy evaluation, which was the secondary objective, was based on the best overall response at the end of the study. Overall, 100 of 120 (83.3%) patients completed the study. Median age of patients was 11 years (range 2-14). Median daily dose of everolimus was 5.82 mg (range 2.0-11.8); median duration of exposure was 56.5 weeks (range 0-130). Overall, AEs were reported in 89 (74.2%) patients; the most common AEs were gynecomastia (18%, 15%), pyrexia (18%, 15%), bronchitis (11%, 9.2%), and asthenia (10.8%). Grade 3 and 4 AEs were reported in 35 (29.2%) and 22 (18.3%) patients, respectively. The most frequent grade 3 AE was stomatitis (4, 3.3%). A total of 62 (51.7%) patients had suspected drug-related AEs, of which 15 (12.5%) were of grade 3 or 4 in 8 (6.7%) patients. AEs caused drug discontinuation. A total of 81 (67.5%) patients had a partial response, 35 (29.2%) patients had a stable disease, and 1 (0.8%) patient had progressive disease. Response was unknown in 2 (1.7%) patients. This study confirms the acceptable safety profile of everolimus in patients with SEGA associated with TSC in a real world setting. Results further support the efficacy of everolimus in the treatment of SEGA associated with TSC.
RESULTS
The study population consists of twenty one MS patients (nine male and twelve female). Median age at presentation was eleven years. In 23.8% of the patients, disease onset was preceded by an infection. One patient (4.8%) had a positive familial history of MS. Serum conversion for Epstein-Barr virus was seen in 93.3%. One third of the patients presented monosymptomatic, 57.1% with vision impairment most frequently due to optic neuritis. An acute disseminated encephalomyelitis-like presentation was seen in 19%. The median time lapse between disease onset and first relapse was eight months, and between disease onset and diagnosis nine months. At diagnosis, all patients had relapsing remitting MS. Median relapse rate was 0.93/year. Most relapses were severe but recovery was complete in most patients. Cerebral MRI at disease onset revealed a median of eight lesions (66.7% juxtacortical, 66.7% infratentorial and 44.4% periventricular). In 19% of the patients, MRI of the spinal cord was performed showing lesions in 75%. In cerebrospinal fluid, white blood cells were increased in 52.6%, IgG-index was increased in 44.4% and oligoclonal bands were detected in 68.4%. Disease modifying therapy was initiated in 71.4% of the patients after a median disease duration of 15.5 months, at a median age of 12.5 years. The median duration of follow-up was 53 months. At last follow-up visit, 19% had reached an EDSS score of three and 9.5% had evolved to secondary progressive MS (SPMS).

CONCLUSIONS
The presented study cohort illustrates the clinical and laboratory features of paediatric MS highlighting a high incidence of positive Epstein-Barr virus serology and the severity of the disease course within 9.5% evolution to SPMS.

ABSTRACT 4
Variable phenotype in epilepsy caused by KCNQ2 mutations

Jansen K., Deremydaeker A., De Waele L., Lagae L.
European Paediatric Neurology Society Congress - May 2015 (Vienna, Austria)

OBJECTIVE
KCNQ2 mutations have been described in infants with benign familial neonatal seizures but also in cases of epileptic encephalopathy. The objective of our study is to investigate the phenotype of KCNQ2-related epilepsy.

METHODS
We reviewed initial seizure types, EEG and MRI data of children with infantile onset epilepsy caused by KCNQ2 mutation followed in the Pediatric Epilepsy Unit in the University Hospitals of Leuven.

RESULTS
We describe 10 infants diagnosed with 9 different heterozygous missense mutations in KCNQ2. Five cases had a familial history of neonatal seizures, 5 cases were de novo. Onset of epilepsy occurred before 2 months in all cases. The predominant seizure type was tonic with deviation of the head and eyes in 6 patients, clonic in 4 patients and co-occurrence of apnea with cyanosis in 4 patients. Normal background EEG was found in 3/5 familial cases. The infants with encephalopathy showed a severely abnormal background activity with a burst-suppression pattern in 2, multifocal epileptic activity in 2 and background EEG in 1 case. Neuro-imaging showed no abnormalities in 9 cases. Normal developmental outcome was seen in 4 familial cases, only 1 had mild developmental delay. The encephalopathies showed moderate developmental delay in 1 and severe developmental delay in 4 cases respectively. All epileptic encephalopathies could initially be classified as drug resistant, but at last follow-up 3 of them were seizure free on medication.

CONCLUSIONS
There is an important phenotypical variability in patients with KCNQ2-related epilepsy. Early start of epilepsy is common, but clinical and electrophysiological phenotype is very variable. Neuro-imaging is not contributive. Familial occurrence has a normal developmental outcome in most cases. The majority of the de novo mutations showed a bad developmental outcome. Our results further suggest that KCNQ2 should be screened for in the diagnostic work-up of early onset intractable seizures.

ABSTRACT 5
Long-term renal outcome of a large cohort of patients with tuberous sclerosis complex

European Renal Association, European Dialysis And Transplant Association Congress - May 2015 (London, UK)

European Society of Paediatric Nephrology Annual Scientific Meeting - September 2015 (Brussels, Belgium)

Tuberous Sclerosis Complex (TSC) is an autosomal dominant neurocutaneous disorder characterized by the growth of hamartomas in multiple organs. Renal involvement represents the second most important cause of morbidity and mortality at all ages, and the most common cause of mortality after the age of 30 years. However, very little is known about the natural history of these renal features in adults and even less in children and adolescents affected by TSC. The purpose of this study is to explore the renal phenotype and long-term renal outcome in a large TSC cohort. We assessed the clinical records and the renal imaging of TSC patients from two tertiary hospitals in a cross-sectional study. Demographics, renal phenotype, renal outcome and co-morbidity data were assessed retrospectively. We included 82 TSC patients, 50 males (61%) with a male/female sex ratio of 1.6. Fifty (61%) patients were younger than 18 years. Median (minimum-maximum) age at last follow-up was 15 (4-72.5) years with a median follow-up duration of 11.1 (0.9-56.6) years. Presenting features (N=69) were neurological complications in 45 (65%) patients and only 4 (6%) patients had renal symptoms as the first clinical sign. TSC1 and TSC2 mutations (N=63) were found in 37 (57%) and 37 (59%) patients respectively. Two patients (3%) had a contiguous gene deletion syndrome. Renal ultrasound at last follow-up (N=64) showed renal angiomyolipomas in 37 (58%) patients and renal cysts in 36 (56%) patients. Renal function (N=72) showed end-stage-renal-disease (ESRD) in 6 (9%) patients with a median age at start of renal replacement therapy of 47.0 (21.0-64.0) years. Estimated glomerular filtration rate (eGFR) was >90 ml/min/m2 in 25 (38%) TSC patients. Three of the 6 patients with ESRD underwent a nephrectomy due to renal cell carcinoma (RCC). Hypertension (N=52), proteinuria (N=31) and renal complications (bleeding, RCC or surgery) were found in 12 (23%), 5 (16%) and 8 (16%) patients respectively. This study describes the long-term renal outcome in a large cohort of TSC patients. Our findings confirm the high rate of renal involvement in TSC. Therefore, we advocate regular renal surveillance of these patients for the timely and optimal managing of the renal co-morbidities.

ABSTRACT 6
Renal features in patients with tuberous sclerosis complex

Verbeke A., Van Husselt S., Van Hoeve K., Levetchenko E., Bammens B., Jansen A., Mekahli D.
European Society of Paediatric Nephrology Annual Scientific Meeting - September 2015 (Brussels, Belgium)
ABSTRACT 1
Association between urinary TIMP-2 and IGFBP7 as early biomarkers of aki and oliguria during liver surgery: a prospective pilot study
Desmet F., D’Hondt M., Callewaert N., Pottel H., Hoste E., Kickum J., De Cort W.
De tekst van het abstract is terug te vinden op p. 10.

PRESENTATIES CONGRESSEN

ABSTRACT 1
In vitro release of cefazolin and vancomycin from three types of impregnated bone chips quantified using UPLC-DAD chromatography
Putzeys G., Boudewyns M., Voet P., Lambrecht S., Croes K.
European Association of Tissue Banks Congress - October 2015 (Split, Croatia)
De tekst van het abstract is terug te vinden op p. 45.

ABSTRACT 2
In vitro release of vancomycin from solution-impregnated bone chips and osteomycin® bonechips quantified using UPLC-DAD chromatography
Putzeys G., Boudewyns M., Voet P., Lambrecht S., Croes K.
European Bone and Joint Infection Association Annual Meeting – September 2015 (Lisboa, Portugal)
De tekst van het abstract is terug te vinden op p. 45.

ABSTRACT 3
Total serum ropivacaine levels after fascia iliaca compartment block with 40mL ropivacaine 0.5%
Van Hoenacker S., Desmet M., Lambrecht S., Croes K., Vermeylen K., Carlier S., Missant C., Van de Velde M.
The European Society of Regional Anaesthesia & Pain Therapy Annual Congress – September 2015 (Ljubljana, Slovenia)
De tekst van het abstract is terug te vinden op p. 14.

ARTIKELS

ABSTRACT 1
Association between urinary TIMP-2 and IGFBP7 as early biomarkers of aki and oliguria during liver surgery: a prospective pilot study
De tekst van het abstract is terug te vinden op p. 10.

ARTIKELS

ABSTRACT 3
Total serum ropivacaine levels after fascia iliaca compartment block with 40mL ropivacaine 0.5%
Van Hoenacker S., Desmet M., Lambrecht S., Croes K., Vermeylen K., Carlier S., Missant C., Van de Velde M.
The European Society of Regional Anaesthesia & Pain Therapy Annual Congress – September 2015 (Ljubljana, Slovenia)
De tekst van het abstract is terug te vinden op p. 14.

KLINISCH LABORATORIUM

Hoarseness Revealing Ortner’s syndrome.
Verbeke X., Vliebergh J., Sauer M., Leys M.
Hoarseness is a common phenomenon that can be caused by uncommon pathology. One seldom cause is Ortner’s syndrome, a rare cardiovascular disease that can lead to hoarseness due to left recurrent laryngeal nerve palsy induced by mechanical compression of the nerve by cardiovascular structures. This case report describes a case of a 41-year-old woman with sudden onset of hoarseness. The patient had known pulmonary hypertension and Eisenmenger’s syndrome.
ABSTRACT 1
A gripping case of peritoneal dialysis catheter malfunction
Doubel P., Vansteenkiste F., Schockaert O.
Kidney Int. 2015 Feb;87(2):483.
A 76-year-old woman with end-stage renal disease was started on peritoneal dialysis using a Swan neck–type catheter. After 1 week of successful peritoneal dialysis, major effluent problems arose. An abdominal X-ray showed the catheter tip being located correctly in the minor pelvis. Empiric attempts to restore catheter function with laxatives and intra-catheter instillation of urokinase failed to improve the effluent flows. A relook laparoscopy showed impingement of the catheter orifices by fimbriae of the right fallopian tube. The catheter was subsequently surgically unobstructed and fixed medially to the anterior abdominal wall, whereas the right ovarium was fixed laterally in the right iliac fossa. Two weeks later, peritoneal dialysis was resumed without any further catheter problems.

Obstruction of the peritoneal dialysis catheter by fallopian tube fimbriae is a rare cause of catheter dysfunction, the more frequent causes being catheter tip migration, entrapment by an omental wrap, or small bowel and fibrin clotting.

ARTIKELS

ABSTRACT 1
Are gadolinium enhanced T1 MR sequences mandatory in the follow up of RRMS patients treated with natalizumab
Seynaeve P., Winnock de Grave P., Claus E., Vandendonckt P., Bourgeois P., Mortele B., Vanovermeire O., Verstraete K.
BACKGROUND
Gadolinium is known to produce side effects and has recently been shown to accumulate in the brain parenchyma especially in the basal ganglia. Since 000 MS patients do undergo several MR examinations, these potential risks have to be considered in this group of patients. Although guidelines advocate the use of gadolinium enhanced imaging in the follow up of RRMS patients, the benefit of the use of gadolinium enhancement in the subgroup treated with natalizumab could be questionable.

METHODS AND MATERIALS
After IRB approval 201 brain scans and 24 spine exams were reviewed in consensus by 3 readers in a series of 27 patients treated with natalizumab (PS, EC, PwdG). These 27 patients were followed during a time span of 6 to 84 months (mean 49 months). Evolution of lesion load and contrast enhancement were scored. Particular interest was given to the diagnosis of PML. The results were compared with the clinical status and the treatment as reported in the patient charts.

RESULTS
Clinical evaluation resulted in 12 episodes of clinical relapse in patients treated with natalizumab, 5 patients demonstrated respectively 1, 2 or 3 relapses. None of the MR scans in the symptomatic patients nor in the asymptomatic patient group demonstrated contrast enhancement. No signs of PML were detected.

CONCLUSIONS
The benefit of T1 MR sequences post contrast as put forward in many guidelines could be questionable in the subgroup of RRMS patients treated with natalizumab.
**ABSTRACT 1**  
Quantification, variability, and reproducibility of basal skeletal muscle glucose uptake in healthy humans using 18F-FDG PET/CT


**RESULTS**  
SUVs in gluteal and quadriceps areas were 0.56 ± 0.09 and 0.64 ± 0.07. ICCs (with 90% confidence intervals) were 0.88 (0.64-0.96) and 0.96 (0.82-0.64). Minimal variability in skeletal muscle glucose uptake was observed under basal conditions in healthy subjects. SUV measurements and rate of glucose uptake values were reproducible, with an average WSCV of less than 5%. Compared with SUV, the 3-tissue model adds information about kinetics between blood, intra- and intercellular compartments, and phosphorylation that may highlight the exact mechanisms of metabolic changes after pharmacologic intervention.

**CONCLUSIONS**  
Minimal variability in skeletal muscle glucose uptake was observed under basal conditions in healthy subjects. SUV measurements and rate of glucose uptake values were reproducible, with an average WSCV of less than 5%. Compared with SUV, the 3-tissue model adds information about kinetics between blood, intra- and intercellular compartments, and phosphorylation that may highlight the exact mechanisms of metabolic changes after pharmacologic intervention.

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**METHODS**  
Six healthy male volunteers underwent 2 dynamic 18F-FDG PET/CT scans with an interval of 24 h. Subjects were admitted to the clinical unit to minimize variability in daily activities and food intake and restrict physical activity. 18F-FDG PET/CT scans of gluteal and quadriceps muscle area were obtained with arterial input. Regions of interest were drawn over the muscle area to obtain time-activity curves and standardized uptake values (SUVs) between 60 and 90 min. Spectral analysis of the data and kinetic modeling was performed using 2-tissue irreversible (2TIR), 2-tissue-reversible, and 3-tissue-segmental irreversible (3TSM) models. Reproducibility was assessed by intra-class correlation coefficients (ICCs) and within-subject coefficient of variation (WSCV).

**RESULTS**  
SUVs in gluteal and quadriceps areas were 0.56 ± 0.09 and 0.64 ± 0.07. ICCs (with 90% confidence intervals) were 0.88 (0.64-0.96) and 0.96 (0.82-0.62), respectively, for gluteal and quadriceps muscles, and WSCV for glucose and quadriceps muscles was 2.2% and 3.5%, respectively. The rate of glucose uptake into muscle was 0.0016 ± 0.0004 mL/mL/min with an ICC of 0.94 (0.93-0.95) and WSCV of 6.6% for the 3TSM model, whereas an ICC of 0.98 (0.92-1.00) and WSCV of 2.8% was observed for the 2TIR model. 3TSMs described the best fit to the measured experimental points.

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Neuromuscul Disord. 2015 May;25(5):381-387.

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**ARTIKELS**

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**ABSTRACT 2**  
Renal function in children and adolescents with Duchenne muscular dystrophy


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**ABSTRACT 3**  
Endothelial Msx1 transduces hemodynamic changes into an arteriogenic remodeling response


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**ABSTRACT 4**  
Sodium iodide symporter PET and BLI noninvasively reveal mesoangioblast survival in dystrophic mice

Holvest B., Quattrocchi M., Belderbos S., Polliaris L., Wolfs E., Gheyens O., Golberg R., Vanrobaek J., Veraille C., Sampaio I., Derese C.

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**ABSTRACT 5**  
How I treat posttransplant lymphoproliferative disorders

Dierickx D., Toussaint T., Gheyens O.

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**ABSTRACT 6**  
Rheumatic fever: a forgotten but still existing cause of fever of unknown origin detected on FDG PET/CT

Salthkke M., Stottz A., Gheyens O.

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**ABSTRACT 7**  
Rheumatic fever: a forgotten but still existing cause of fever of unknown origin detected on FDG PET/CT

Salthkke M., Stottz A., Gheyens O.

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**ABSTRACT 8**  
Rheumatic fever: a forgotten but still existing cause of fever of unknown origin detected on FDG PET/CT

Salthkke M., Stottz A., Gheyens O.

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**ABSTRACT 9**  
Rheumatic fever: a forgotten but still existing cause of fever of unknown origin detected on FDG PET/CT

Salthkke M., Stottz A., Gheyens O.
candidiasis. This case illustrates that rhabdomyosarcoma can be detected on 18F-FDG PET/CT and demonstrates the value of 18F-FDG PET/CT in patients with fever of unknown origin.

ABSTRACT 7
Asymmetric pulmonary hypermetabolism on 18F-FDG PET/CT caused by pulmonary embolism
Casselaere E., Derouze C., Verhamme P., Coolen J., Gheysens O.
We present a case of diffuse and moderately increased 18F-FDG uptake in the entire left lung on 18F-FDG PET without any morphological parenchymal abnormalities in a patient with recent history of esophageal adenocarcinoma treated by minimal invasive surgery and adjuvant chemotherapy. Contrast-enhanced CT revealed a large embolism in the left pulmonary artery with near total occlusion. In the absence of parenchymal lesions, the increased 18F-FDG uptake is most likely an inflammatory response to a recent ischemic insult. This case illustrates that asymmetric lung hypermetabolism in the absence of parenchymal disease can be caused by a central pulmonary embolism.

ABSTRACT 8
The reproducibility of MTV PET based metabolic tumor volume measurements and of their FDG distribution within

AIM
The aim of this study was to report on the reproducibility of 18F-Fluorodeoxyglucose (FDG) PET/CT (99m)Tc-annexin A5 uptake in patients with lung cancer and squamous cell carcinoma of the head and neck (SCCHN).

METHODS
Nineteen patients (14 men) who underwent a baseline staging FDG PET-CT examination and a second radio-
therapy treatment planning FDG PET-CT examination prior to treatment initiation within 27 days (range: 7-37 days) from each other were included. Bland-Altman analysis was performed on MTV40% and MTVSUv2.5 2.5 volumes obtained of the primary tumor. For voxelwise comparison of the FDG distribution within tumors the transformation matrix, defined on the CT images, was applied to the corresponding FDG images. Accordingly, the MTV40% of the primary tumor volume was defined and copied on the second FDG image. The coordinates and SUV values of each pixel in the corresponding volumes in both FDG images were used for paired comparison.

RESULTS
The standard deviation of the percentage spread around the means of both measurements was respectively 32.5% for MTVSUv2.5 versus 18.8% for MTV40%. Using a cut-off value of 1.96 SD, differences exceeding 64% in MTVSUv2.5 and 37% in MTV40% may be considered to be clinically relevant. Correlation coefficients derived from the voxelwise paired comparison of SUV values within MTV40% volumes delineated on scan 1 and scan 2 ranged from 0.67 to 0.96 (mean: 0.83). Bland-Altman plots demonstrated a low reproducibility for low SUV values and a high(er) reproducibility for high SUV values (inverted triangular shape) in all tumor volumes under study.

CONCLUSIONS
The reproducibility of MTV40% proved better than that of MTVSUv2.5 with a cut-off of 3% (increase or decrease) in MTV allowing to define clinically significant changes. Furthermore, the intravoxel FDG distribution did not change significantly in most of the patients during the time interval studied.

ABSTRACT 9
Crosstalk between the microbiome and cancer cells by quorum sensing peptides

To date, the precise role of the human microbiome in health and disease states remains largely undefined. Complex and selective crosstalk systems between the microbiome and mammalian cells are also not yet reported.

Research up till now mainly focused on bacterial synthesis of virulence factors, reactive oxygen/hydrogen species (ROS/RNS) and hydrogen sulphide, as well as on the activation of exogenous mutagen precursors by intestinal bacteria. We discovered that certain quorum sensing peptides, produced within bacteria, interact with mammalian cells, in case cancer cells: Phr0662 (Bacillus sp.), Enf-metabolite (Enterococcus faecium) and EDF-derived (Escherichia coli) peptides initiate HCT-8/E11 colon cancer cell invasion, with Phr0662 also promoting angiogenesis. Our findings thus indicate that the human microbiome, through their quorum sensing peptides, may be one of the factors responsible for cancer metastasis.

ABSTRACT 10
The quorum sensing peptides PhrG, Csf and EDF promote angiogenesis and invasion of breast cancer cells in vitro

The role of the human microbiome on cancer progression remains unclear. Therefore, in this study, we investigated the influence of some quorum sensing peptides, produced by diverse commensal or pathogenic bacteria, on breast cancer cell invasion and thus cancer outcome. Based on microscopy, transcriptomics and ChIP-Chrino-Atlantic Membrane (CAM) analyses, four peptides (PhRG from B. subtillis, CsfP from S. mitis and EDF from E. coli, together with its tripeptide analogue) were found to promote tumor cell invasion and angiogenesis, thereby potentially influencing tumour metastasis. Our results offer not only new insights on the possible role of the microbiome in health and disease states, but may open new opportunities in cancer prevention and therapy by combating these endogenous molecules and/or by modifying people’s lifestyle.

ABSTRACT 11
(99m)Tc-Annexin A5 quantification of apoptotic tumor response: a systematic review and meta-analysis of clinical imaging trials

Belhocine T., Blankenberg F., Kartachova M., Stitt L., Vanderheyden J., Hoebers F., Van de Wiele C.
PURPOSE
(99mTc)-Annexin A5 has been used as a molecular imaging probe for the visualization, characterization and measurement of apoptosis. In an effort to define the quantitative (99mTc)-annexin A5 uptake criteria that best predict tumor response to treatment, we performed a systematic review and meta-analysis of the results of all clinical imaging trials found in the literature or publicly available databases.

METHODS
Included in this review were 17 clinical trials investigating quantitative (99mTc)-annexin A5 (qAnx5) imaging using different parameters in cancer patients before and after the first course of chemotherapy and/or radiation therapy. Qualitative assessment of the clinical studies for diagnostic accuracy was performed using the QUADAS-2 criteria. Of these studies, five prospective single-center clinical trials (92 patients in total) were included in the meta-analyses after exclusion of one multicenter clinical trial due to heterogeneity. Pooled positive predictive values (PPV) and pooled negative predictive values (NPV) (with 95% CI) were calculated using Meta-Disco software version 1.4.

RESULTS
Absolute quantification and/or relative quantification of (99mTc)-annexin A5 uptake were performed at baseline and after the start of treatment. Various quantitative parameters have been used for the calculation of (99mTc)-annexin A5 tumor uptake and delta (Δ) tumor changes post-treatment compared to baseline including: tumor-to-background ratio (TBR), STU (tumor-to-noise ratio), absolute tumor ratio (TR), STU (standardized tumor uptake ratio (STU), Δ STU, maximum count per pixel within the tumor volume (%max). Emami, absolute ΔSU and percentage (%ΔSU), maximum ΔSU counts, semiquantitative visual scoring, percent injected dose (%ID) and %ID/cm(3). Clinical trials investigating qAnx5 imaging have included patients with lung cancer, breast cancer, head and neck cancer and other less common tumor types. In two phase I/II single-center clinical trials, an increase of ≥25% in uptake following treatment was considered a significant threshold for an apoptotic tumor response (partial response, complete response). In three other phase I/I clinical trials, increases of ≥25%, ≥42% and ≥47% in uptake following treatment were found to be the mean cut-off levels in responders. In a phase II/III multicenter clinical trial, an increase of ≥23% in uptake following treatment was found to be the minimum cut-off level for a tumor response. In one clinical trial, no significant difference in (99mTc)-annexin A5
uptake in terms of %ID was found in healthy tissues after chemotherapy compared to baseline.

In two other clinical trials, intraserver and interobserver-verification measurements of (99m)Tc-annexin A5 tumor uptake were found to be reproducible (mean difference 0%, kappa = 0.90 ± 0.04; r = 0.82; respectively) and to be highly correlated with treatment outcome (p = 0.0001).

The meta-analysis demonstrated a pooled positive PPV of 70% (55% CI 52 - 100%) and a pooled negative NPV of 70% (95% CI 11 - 82%) for prediction of a tumor response after the first course of chemotherapy and/or radiotherapy in terms of %ID. In a symmetric IARC analysis, the AUC was 0.919 and the Q index was 85.21%.

CONCLUSIONS
Quantitative (99m)Tc-annexin A5 imaging has been investigated in clinical trials for the assessment of apoptotic tumor responses. This meta-analysis showed a high pooled PPV and a moderate pooled NPV with 70% cut-off values ranging between 20% and 30%.

Standardization of quantification and harmonization of results are required for high-quality clinical research. A standardized uptake value score (SUV, SUVmax) using quantitative SPECT/CT imaging may be a promising approach to the simple, reproducible and semiautomatic assessment of apoptotic tumor changes.

PRESENTATIES CONGRESSEN

ABSTRACT 12
Quorum Sensing Peptides Selectively Penetrate the Blood-Brain Barrier

Bacteria communicate with each other by the use of signaling molecules, a process called ‘quorum sensing’. One group of quorum sensing molecules includes the oligopeptides, which are mainly produced by Gram-positive bacteria. Recently, these quorum sensing peptides were found to be biologically inﬂuence human mammalian cells, promoting i.a. metastasis of cancer cells. Moreover, it were found to biologically influence mammalian cells, oligopeptides, which are mainly produced by Gram-po signaling molecules, a process called ‘quorum sensing’.

Here, three chemically diverse quorum sensing pep-
tides were investigated for their brain inﬂux (multiple time regime biological) and eﬄux properties in an in vivo mouse model (ICR-CD-1) to determine blood-brain transfer properties. PhrCAT1 demonstrated comparably very high initial inﬂux into the mouse brain (Kin = 20.87 μl/g(min)), while brain penetrabilities of BIP-2 and PhrANTH2 were found to be low (Kin = 6.8 μl/g(mnin)) and very low (Kin = 0.18 μl/g(min)); respectively. All three peptide sequences were metabolically stable in plasma (in vitro) during the experimental time frame and no significant brain eﬄux was observed.

Initial tissue distribution data showed remarkably high liver accumulation of BIP-2 as well. Our results thus support the potential role of some quorum sensing peptides in diﬀerent neurological disorders, thereby enlarging our knowledge about the microbiome-brain axis.

ABSTRACT 1
Automated dispensing and injection of 18F-FDG decreases personnel radiation burden

AIM
In nuclear medicine departments with a positron emission tomography (PET) system, the personnel doses have increased over the last decade due to an increasing number of PET procedures. In az groeninge, the increasing personnel dose emphasized the need for optimizing the individual workload in order to keep the radiation exposure as low as possible. Therefore, an automated dispensing and injection system was installed and an additional PET shift was implemented. The aim of our study was to evaluate the personnel whole-body and extremity doses after implementation of the extra shift and automated infusion system in comparison to historical data.

MATERIALS AND METHODS
A Medrad Intego™ automated dispensing and injection system was used to administer 18F-fluoro-deoxyglucose (FDG) to the patients.

Personnel doses were evaluated using a breast dosimetre- ter provided by AIIB Vincotte Controlatom. Both types of dosimeters are thermo luminescence dosimeters (TLD’s), that were read out monthly. The radiation dose per PET shift was calculated because not everybody had the same number of PET shifts every month.

RESULTS
The reference value of the whole-body and extremity dose is respectively 38.48 μSv and 377.48 μSv per PET shift. After implementation of the extra PET shift (in casu 3 PET shifts instead of 2 shifts per day) the extremity dose decreased to 254.85 μSv per PET shift (32.5% reduction), whereas the whole-body dose remained constant (40.90 μSv per PET shift). The second optimisation strategy, consisting of using the automated dispensing and injection system, thus decreased to 154.66 μSv per PET shift (59.03% reduction).

CONCLUSIONS
In az groeninge, the personnel radiation burden has decreased by adding an extra shift for PET examinations and by using an automated dispensing and injection system. Optimizing radiation burden is an ongoing process and further analyses are necessary to keep decreasing the personnel whole-body and extremity dose.

ABSTRACT 2
Preclinical validation of automated DXA- and CT-based body composition measurements
Devries J., Beels L., Maes A., Van de Wiele C., Potthof H.
European Association of Nuclear Medicine Annual congress – October 2015 (Hamburg, Germany)

AIM
A Medrad Intego™ automated dispensing and injection system was used to administer 18F-fluoro-deoxyglucose (FDG) to the patients.

Preclinical validation performed using small animal images and literature HU ranges showed small differences from true mass, while total mass DXA measurements differed more from true mass. Therefore, automated tissue segmentation using CT images and a solid set of Hounsfield unit (HU) ranges is possible through calculation of the standardized uptake value (SUV), which is defined as the ratio of measured radioactivity concentration to the injected dose per unit of volume of distribution. SUV is traditionally normalized for body weight. Lean body mass (LBM) has also been proposed as volume of distribution, since e.g. 18F-FDG distribution in fatty tissues is limited, and the use of LBM-normalized SUV is gaining popularity. LBM can be estimated by predicative equations, or measured by e.g. dual-energy X-ray absorptiometry (DXA) or computed tomography (CT). If SUV would be possible to obtain an accurate SUV measurement from a DXA scan or CT scan, accurate and reproducible LBM-normalized SUVs could be calculated.

The purpose of this study is to determine and validate a set of Hounsfield unit (HU) ranges to segment CT images into tissue types and to test the validity of DXA tissue segmentation on pure, unmixed porcine tissues.

MATERIALS AND METHODS
This preclinical prospective study was approved by the local ethical committee. Different quantities of porcine bone tissue (BT), lean tissue (LT) and adipose tissue (AT) were scanned using DXA and CT. Tissue type segmentation in DXA was performed via the standard clinical protocol and in CT through different sets of HU ranges. Percent coefficients of variation (%CV) were used to assess precision while % differences of observed masses were tested against zero using the Wilcoxon signed-rank test.

RESULTS
Total mass DXA measurements differ little but signifi-
cantly (p<0.016) from true mass, while total mass CT measurements based on literature HU ranges show non-significant (p>0.05) differences of 1.7% and 2.0%. CT mass estimates with DXA differed more from true mass (median -78.2 to -75.8%) than other tissue types (median -11.3 to -8.1%). Tissue mass estimates with CT and literature HU ranges showed small differences from true mass for every tissue type (median -10.4 to 6.8%).
ARTIKELS

ABSTRACT 1

G-8 indicates overall and quality-adjusted survival in older head and neck cancer patients treated with curative radiochemotherapy

Debruyne P.

BACKGROUND

Evidence-based guidelines concerning the older head and neck cancer (HNCA) patient are lacking. Accurate patient selection for optimal care management is therefore challenging. We examined if geriatric assessment is indicative of long-term health-related quality of life (HRQOL) and overall survival in this unique population.

METHODS

All HNCA patients, aged ≥65 years, eligible for curative radiochemotherapy were evaluated with the Geriatric Risk Assessment (G-8) and a comprehensive geriatric assessment (CGA). Europ-5 dimensions (EQ-5D) and survival were collected until 36 months post treatment start. Repeated measures ANOVA was applied to analyse HRQOL evolution in fit and ‘vulnerable’ patients, defined by G-8. Kaplan-Meier curves and Cox proportional hazard analysis were determined for the prognostic value of geriatric assessments. Quality-adjusted survival was calculated in both patient subgroups.

RESULTS

One hundred patients were recruited. Seventy-two percent of patients were considered vulnerable according to CGA (≥2 abnormal tests). Fit patients maintained a relatively less remaining life months in perfect health in vulnerable patients. A similar trend was seen based on CGA. median health states. The difference remained apparent at 36 months. Vulnerability, defined by G-8, is indicative of quality-adjusted survival, and should be considered at time of treatment decisions for the older HNCA patient.

CONCLUSIONS

G-8 is indicative of quality-adjusted survival, and should be considered at time of treatment decisions for the older HNCA patient.

ABSTRACT 2

Phase II study of weekly paclitaxel/carboplatin in combination with prophylactic G-CSF in the treatment of gynecologic cancers: a study in 108 patients by the Belgian Gynaecological Oncology Group


OBJECTIVE

To investigate the addition of prophylactic G-CSF to each weekly paclitaxel/carboplatin course in patients with recurrent platinum-resistant ovarian (OC), or recurrent or advanced endometrial (EC) or cervical carcinoma (CC).

METHODS

108 patients were enrolled i.e. 36 in each cohort. Eighteen courses of paclitaxel (60 mg/m2) and carboplatin (AUC 2.7) were administered weekly. G-CSF (Neupleride) was given to all patients on day 5 (and if needed on day 6).

RESULTS

For patients with OC, 91% had platinum-resistant and 9% platinum-refractory disease. Median number of prior chemotherapy lines was 3 for OC, 1 for EC, and 3 for CC. Grade 3-4 neutropenia was observed in 34% of patients (95% CI: 26-44%). Confirmed sepsis was observed in 5% of patients. Grade 3-4 thrombocytopenia was observed in 43% (95% CI: 32-54%). Median (95% CI) 28-36 months, respectively (OC 7 and 13, EC 6 and 19, CC 6 and 14).

CONCLUSIONS

Weekly paclitaxel/carboplatin with G-CSF is an effective treatment with acceptable toxicity in patients with platinum-resistant or platinum-refractory OC, advanced or recurrent EC and CC. The incidence of grade 3-4 neutropenia is lower with the addition of weekly G-CSF compared with earlier studies without routine use of prophylactic G-CSF.

ABSTRACT 3

Genetic variability in drug transport, metabolism or DNA repair affecting toxicity of chemotherapy in ovarian cancer

Belgian and Luxembourg Gynaecological Oncology Group (BGOG).

BACKGROUND

This study aimed to determine whether single nucleotide polymorphisms (SNPs) in genes involved in DNA repair or metabolism of taxanes or platinum could predict toxicity or response to first-line chemotherapy in ovarian cancer.

METHODS

Twenty-six selected SNPs in 18 genes were genotyped in 322 patients treated with first-line paclitaxel/carboplatin or carboplatin monotherapy. Genotypes were correlated with toxicity events (anemia, neutropenia, thrombocytopenia, febrile neutropenia, neurotoxicity). Use of growth factors and survival.

RESULTS

The risk of anemia was increased for variant alleles of rs1126503 (ABCB1, C > T; p = 0.023, OR = 1.71, 95% CI = 1.07-2.71), rs633717 (ABCA1, A > G; p = 0.002, OR = 2.06, 95% CI = 1.32-3.27) and rs11515 (ERCC1, C > T; p = 0.031, OR = 1.61, 95% CI = 1.04-2.50), which was decreased for variant alleles of rs377625490 (ABCC2, C > G; p = 0.004, OR = 0.51, 95% CI = 0.33-0.81). Likewise, increased risk of thrombocytopenia was associated with the use of colony stimulating factors (CSF), while rs2074087 (ABCC1, G > C; p = 0.011, OR = 2.03, 95% CI = 1.16-3.58) correlated with use of erythropoiesis stimulating agents (ESA). rs1799793 (ERCC2, G > A) allele had a prolonged platinum-free interval (p = 0.026).

CONCLUSIONS

Our data reveal significant correlations between genetic variants of transport, hepatic metabolism, platinum related detoxification or DNA repair damage and toxicity or outcome in ovarian cancer.

ABSTRACT 4

Integration of geriatric oncology in daily multidisciplinary cancer care: the time is now


Editorial without abstract.

ABSTRACT 5

Optimisation of pharmacy content in clinical cancer research protocols: experience of the United Kingdom chemotherapy and pharmacy advisory service


BACKGROUND

Clarity and accuracy of the pharmacy aspects of cancer clinical trial protocols is essential. Inconsistencies and ambiguities in such protocols have the potential to delay research and jeopardise both patient safety and collection of credible data. The Chemotherapy and Pharmacy Advisory Service was established by the UK National Cancer Research Network, currently known as National Institute for Health Research Clinical Research Network, to improve the quality of pharmacy-related content in cancer clinical research protocols. This article reports the scope of Chemotherapy and Pharmacy Advisory Service, its methodology of mandated protocol review and pharmacy-related guidance initiatives and its current impact.
METHODS
Over a 6-year period (2009-2013) since the inception of Chemotherapy and Pharmacy Advisory Service, cancer clinical trials protocols were reviewed by the service, prior to implementation at clinical trial sites. A customised Review Checklist was developed and used by a panel of experts to standardise the review process and report back queries and inconsistencies to chief investigators. Based on common queries, a Standard Protocol Template comprising specific guidance on drug-related content and a Pharmacy Manual Template were developed. In addition, a guidance framework was established to address ‘ad hoc’ pharmacy-related queries. The most common remarks made at protocol review have been summarised and categorised through retrospective analysis. In order to evaluate the impact of the service, we have received a list of all notes and remarks that investigators were asked to respond to queries made at protocol review and make appropriate changes to their protocols. Responses from chief investigators have been collated and acceptance rates determined.

RESULTS
A total of 176 protocols were reviewed. The median number of remarks per protocol was 26, of which 20 were deemed clinically relevant and mainly concerned the drug regimen, support medication, frequency and type of monitoring and drug supply aspects. Further analysis revealed that 62% of chief investigators responded to the review. All responses were positive with an overall acceptance rate of 89% of the proposed protocol changes.

CONCLUSIONS
Review of pharmacy content of cancer clinical trial protocols is feasible and exposes many undetected clinically relevant issues that could hinder efficient trial conduct. Our service audit revealed that the majority of suggestions were effectively incorporated in the final protocols. The refinement of existing and development of new pharmacology guidance documents by Chemotherapy and Pharmacy Advisory Service might aid in better and safer outcomes.

ABSTRACT 6
Outcomes from second-line therapy in long-term responders to first-line tyrosine kinase inhibitor in clear-cell metastatic renal cell carcinoma

BACKGROUND
Although sequential targeted therapy is standard in patients with metastatic renal cell carcinoma (m-ccRCC), the choice of drugs and optimal administration sequence have yet to be established. The objective of this study was to explore whether it is preferable to rechallenge a long-term responder to a first-line tyrosine kinase inhibitor (TKI) with a TKI or whether to switch to a mammalian target of rapamycin inhibitor (mTORi), to determine whether second-line treatment response depends on duration of first-line treatment (TD1). PA- TIENTS AND METHODS: Retrospective multicenter study (2004-2011) of 243 consecutive mRCC patients (clear-cell histology) who received a first-line TKI for 26 months followed by a second-line TKI (n = 118) or mTORi (n = 123).

END POINTS
Progression-free survival (PFS) and time-to-treatment failure (TTF) on second-line therapy. Multivariable full-model: second-line drug, TD1, ECOG-PS before first- and second-line, best objective response (first-line), Fuhrman grade, number of metastatic sites, and presence of bone metastases. Adjustment covariable: International mRCC Database Consortium (IMDC) risk score. Multiple propensity score and missing data methods were used. Any correlation between first-line and second-line PFS was investigated using censored quantile regression models (CQR).

RESULTS
Sequence effect in the overall cohort was in favor of the TKI-TKI sequence over the TKI-mTORi sequence on using chemotherapy pathways. In this paper we present recommendations based on a thorough review of available guidelines and data from the phase III randomised controlled trials that evaluated new agents in patients with advanced metastatic renal cancer.

ABSTRACT 7
Management and systemic treatment of clear cell metastatic renal cell carcinoma: BSMO expert panel recommendations

BSMO Renal Task Force Group.

Almost 30% of patients with renal cell cancer present initially with advanced stage IV disease. In the past decade, the management of the metastatic renal cell cancer has been revolutionised by the knowledge of its molecular biology and development of targets against vascular endothelial growth factor and mammalian target of rapamycin pathways. In this paper we present recommendations based on a thorough review of available guidelines and data from the phase III randomised controlled trials that evaluated new agents in patients with advanced metastatic renal cancer.

ABSTRACT 8
Erlotinib plantagineum (echium) does not prevent weight loss in head and neck cancer patients

Wieder B., Pottlo L., Debruyne P.

BACKGROUND
The effect of internal mammary and medial supraclavicular lymph-node irradiation (regional nodal irradiation) added to whole-breast or thoracic-wall irradiation after surgery on survival among women with early-stage breast cancer is unknown.

METHODS
We randomly assigned women who had a centrally or medially located primary tumor, irrespective of axillary involvement, or an externally located tumor with axillary involvement to undergo either whole-breast or thoracic-wall irradiation (regional nodal irradiation) added to whole-breast or thoracic-wall irradiation after surgery (control group). The primary end point was overall survival. Secondary end points were the rates of disease-free survival, survival free from distant disease, and death from breast cancer.

RESULTS
Between 1996 and 2004, a total of 4004 patients underwent randomization. The majority of patients (76.1%) underwent breast-conserving surgery. After mastectomy, 73.4% of the patients had received adjuvant systemic treatment and 26.6% had undergone additional treatment, of whom 97% received adjuvant chemotherapy, and 5% radiotherapy. Median follow-up of 10.9 years, 811 patients had died. At 10 years, overall survival was 82.3% in the nodal-irradiation group and 80.7% in the control group (hazard ratio for death with nodal irradiation, 0.87; 95% confidence interval [CI], 0.76 to 1.00; P = 0.06). The rate of disease-free survival was 72.1% in the nodal-irradiation group and 69.1% in the control group (hazard ratio for disease progression or death, 0.89; 95% CI, 0.80 to 1.00; P = 0.04; the rate of disease-free survival was

ABSTRACT 9
Internal mammary and medial supraclavicular irradiation in breast cancer


BACKGROUND
This study was to explore whether it is preferable to add internal mammary and medial supraclavicular irradiation (IM & MS) to whole-breast or thoracic-wall irradiation after surgery for breast cancer.

METHODS
We randomly assigned women who had a centrally or medially located primary tumor, irrespective of axillary involvement, or an externally located tumor with axillary involvement to undergo either whole-breast or thoracic-wall irradiation (regional nodal irradiation) added to whole-breast or thoracic-wall irradiation after surgery (control group). The primary end point was overall survival. Secondary end points were the rates of disease-free survival, survival free from distant disease, and death from breast cancer.

RESULTS
Between 1996 and 2004, a total of 4004 patients underwent randomization. The majority of patients (76.1%) underwent breast-conserving surgery. After mastectomy, 73.4% of the patients had received adjuvant systemic treatment and 26.6% had undergone additional treatment, of whom 97% received adjuvant chemotherapy, and 5% radiotherapy. Median follow-up of 10.9 years, 811 patients had died. At 10 years, overall survival was 82.3% in the nodal-irradiation group and 80.7% in the control group (hazard ratio for death with nodal irradiation, 0.87; 95% confidence interval [CI], 0.76 to 1.00; P = 0.06). The rate of disease-free survival was 72.1% in the nodal-irradiation group and 69.1% in the control group (hazard ratio for disease progression or death, 0.89; 95% CI, 0.80 to 1.00; P = 0.04; the rate of disease-free survival was...
Mycelofibrosis patients in Belgium: disease characteristics


ACTA CLIN BELG. 2015 Apr;70(2):105-111.

OBJECTIVE

To date, only a small number of epidemiological studies on myelofibrosis have been performed. The current study aimed to characterize the myelofibrosis patient population in Belgium according to pre-defined disease parameters (diagnosis, risk categories, hemoglobin <10 g/dl, spleen size, constitutional symptoms, platelet count, myeloblast count), with a view to obtaining a deeper understanding of the proportion of patients that may benefit from the novel myelofibrosis therapeutic strategies.

METHODS

A survey was used to collect data on prevalence and disease parameters on all myelofibrosis patients seen at each of 18 participating hematologic centers in 2011. From November 2012 till February 2015, 8467 patients were included. Median age was 78.7 years (range: 70–101), and 70% had an abnormal G8 score warranting a GA. In the group of patients were GA was performed, geriatric recommendations were given to 39.0 % of the patients. The final database is currently being constructed, and results on all the endpoints will be provided at the meeting.

RESULTS

A total of 250 patients with myelofibrosis were captured; of these, 136 (54%) were male and 153 (61%) were over 65 years old. One hundred sixty-five (66%) of myelofibrosis patients (77%) had a palpable spleen. About a third of patients (34%) suffered from constitutional symptoms. Two hundred twenty-two (89%) myelofibrosis patients had platelet count ≥50 000/μl and 201 (80%) had platelet count ≥100 000/μl. Of 250 patients, 85 (34%) had a myeloblast count ≥1%. Six (2%) patients had undergone a splenectomy. Thirteen (5 2%) patients had undergone radiotherapy for splenomegaly.

CONCLUSIONS

The results of this survey provide insight into the characteristics of the Belgian myelofibrosis population. They also suggest that a large proportion of these patients could stand to benefit from the therapies currently under development.

PRESENTATIES CONGRESSEN

ABSTRACT 10

A nationwide implementation of a multidisciplinary geriatric assessment and intervention program in Belgian older patients with cancer


NATIONAL CANCER INSTITUTE – Prague, Czech Republic

INTRODUCTION

In the general older population, Comprehensive Geriatric Assessment (GA)-guided treatment plans improve overall survival (OS), quality of life (QoL), and functional status (FS) and decrease the risk of unplanned hospital readmissions and institutionalization. In oncology, GA research has mainly studied the diagnostic process of geriatric screening and assessment and has not yet thoroughly focused on geriatric interventions and follow-up.

OBJECTIVE

The objective of this study was to implement geriatric assessment and interventions nationwide within the Belgian older population with cancer in collaboration with geriatricians and the Belgian geriatric care program. More specifically, geriatric screening, GA, geriatric recommendations, interventions and follow-up were tested in a realistic and implementable manner.

METHODS

With financial support of the Belgian Cancer Plan, a prospective multicenter (n=22) cohort study was initiated in order to implement the above mentioned steps of a GA process in each participating center. Eligible patients had an invasive cancer or hematologic malignancy, were ≥70 years old and an oncologic treatment decision had to be made. At baseline, patients were screened using G8 and if abnormal (score ≤14/17), a GA was performed. Geriatric recommendations for interventions were formulated by a trained health care worker (THCW), in collaboration with the geriatric care program (e.g. inpatient geriatric consultation team or geriatric day clinic). About 3 months after baseline assessment, the general health status of the older patient was reassessed and unplanned readmissions, survival, and performance of the proposed geriatric recommendations were documented. The endpoints were: “What are the geriatric recommendations proposed based on the GA?” “How much of these recommendations have been carried out at (3 months) follow-up?” How often have established parts of the geriatric care program (e.g. geriatric day clinic, fall clinic) been used? How often have referrals to other health care workers (e.g. psychologists, dieticians, social workers) been established? What kind of additional health problems occur at (3 months) follow-up? How many unplanned readmissions to the hospital were identified and what were the reasons for unplanned readmissions during follow-up?

RESULTS

From November 2012 till February 2015, 8467 patients were included. Median age was 78.7 years (range: 70–101), and 70% had an abnormal G8 score warranting a GA. In the group of patients were GA was performed, geriatric recommendations were given to 39.0 % of the patients. The final database is currently being constructed, and results on all the endpoints will be provided at the meeting.

CONCLUSIONS

This nationwide implementation project evaluated 8467 older patients with cancer in 2.5 years in a uniform way. The close collaboration with geriatricians and the Belgian geriatric care program corresponds well to the authorities’ vision that oncology should not develop geriatric programs independently from the Belgian geriatric care program. It is expected that involvement of geriatric expertise in a uniform national strategy, will improve cancer treatment decisions and health care in general for older patients with cancer, possibly leading to cost reductions since treatments can be tailored for each individual.
OBJECTIVES

The objective of this study is 2-fold: to assess the influence of wrist position on maximum grip force generated in a post-operative orthosis and to determine the correlation between this maximum grip force and an individual’s grip strength.

STUDY DESIGN

Clinical measurement METHODS: A total of 30 uninjured wrists of right-handed men were given post-operative orthosis with an incorporated Carolintheses. The maximum grip force was measured according to a different wrist position ranging from ‘30° extension until 80° of flexion using a 10° interval. These measurements were plotted out on a graph for regression analysis. A correlation was determined between measurements in a neutral wrist position and maximum grip strength generated without an orthosis. To assess the coherence of the measurements, a mean intraclass correlation coefficient was used.

RESULTS

The maximum grip force values were statistically significantly different in every wrist position and decreased progressively with an increasing flexion angle (p < 0.05). This relationship is expressed in a logistic regression curve (f(x) = -4.98 + 16.02 (1 / 1 + e^(-5.92)(2.24). A wrist position of 4° of flexion was derived from this function to cause a maximum grip force reduction of 33%. Further analysis showed a force decrease of 50% at 23.2° and 66% at 51.8° of wrist flexion. The grip strength measured without an orthosis showed a positive correlation with previous measurements (Spearmen’s correlation coefficient = 0.34 for the right hand and 0.72 for the left hand (p = 0.001)).

CONCLUSIONS

The obtained logistic function allowed to derive the wrist position needed in a post-operative orthosis to obtain a desired amount of maximum grip force reduction.

CLINICAL RELEVANCE

Measuring a high grip force in a clinical setting of flexor tendon repair on the centralateral non-affected hand could indicate the use of an increased flexion angle in a post-operative orthosis. This reduces the load transferred on the tendon repair when involuntary contractions take place, for example, during sleeping when positioned in a post-operative orthosis.

ABSTRACT 2

Percutaneous bunionette correction: a cadaveric study


PURPOSE

The purpose of this study was to evaluate a percutaneous technique to treat a bunionette deformity.

METHODS

Twenty-four lower extremity cadaveric specimens were processed lyophilized bonechips (BCs). Quantification was performed using a fully validated chromatographic method, enabling measurement of the concentration of minimum 100 mg/mL during 10 minutes. It has been shown that a concentration of 20 mg/mL for 24 hours is mandatory to obtain better AB-impregnated BC carriers.

RESULTS

The linear-elution window for VAN was 25-1000 mg/L for 3 days. Longer impregnation time at this concentration had no effect. Osteomycin® delivers the desired local concentration for 8 days in our experimental setting.

DISCUSSION AND CONCLUSIONS

Literature suggests that fresh-frozen BCs can be used as carrier for CFZ and VAN. Due to limited knowledge of their release characteristics from processed BCs we performed elution studies on processed BCs compared with fresh-frozen BCs and a commercial product. To facilitate comparison, our protocol was based on that of Mathyssen et al., but with direct quantification of elution concentrations. In contrast to the results of Mathyssen et al., the impregnation concentration had to be increased to 20 mg/mL to reach the desired local concentration which is however reached for only 4 hours. Impregnation with VAN 100 mg/mL during 10 minutes results in a release above the desired concentration for 3 days. Osteomycin® shows a substantially longer elution. Further research is mandatory to obtain better AB-impregnated BC carriers.

ABSTRACT 3

In vitro release of cefazolin and vancomycin from three types of impregnated bone chips quantified using UPLC-DAD chromatography

Putzeys G., Boudewijns M., Voet P., Lambrecht S., Croos K. European Association of Tissue Banks Congress - October 2015 (Split, Croatia)

INTRODUCTION

Antibiotic (AB)-impregnated bonechips from a human morselized femoral head allograft (BCs) are widely used in orthopaedic surgery to prevent or treat infections. Literature suggests that BCs are efficient carriers, but due to the diversity in the type of ABs, of BCs and of method used to evaluate AB release, a uniform impregnation protocol has not been draughted for. In our hospital, a protocol on the use of AB-impregnated BCs was introduced based upon literature data with cefazolin (CFZ) as prophylactic AB and vancomycin (VAN) as document AB treat- ment. However, as no studies have been performed with the type of BC used in our hospital and only limited data are available for CFZ, we performed an in vitro study to examine the release of both Abs from these impregnated BCs. Quantification was performed using a fully validated chromatographic method.

METHODS

For CFZ, impregnation with varying concentrations (0.2; 2; 20 and 200 mg/mL), durations (10, 30 and 240 min) and types of BCs (Fresh frozen, processed frozen and processed lyophilized bonechips) was performed; for VAN only the impregnation concentration and duration were investigated. After impregnation, BCs were rinsed with saline in order to determine only the absorbed AB. Elution was performed in newborn calf serum at 37°C. Eluted AB concentrations were determined using Ultra Performance Liquid Chromatography – Diode Array Detection (UPLC- DAD). This chromatographic method, enabling measurement of VAN and CFZ, was fully validated according to FDA-criteria. In addition an elution study was performed on the commercially available Osteomycin®, bone chips containing VAN.

RESULTS

CFZ: In vitro experiments suggest that an impregnation concentration of 20 mg/mL is optimal, that AB uptake increases with impregnation time and that frozen BCs release significantly more AB than lyophilized. Frozen BCs impregnated with 20 mg/mL CFZ for 4 hours deliver the desired local concentration (therapeutic window 2 – 200 mg/L) for max. 4 hours, independent of the BC type (fresh frozen vs processed frozen). Fresh-frozen BCs elute significantly more within the first 2 hours.

VAN: using processed frozen BCs, an impregnation-con- centration of minimum 100 mg/mL during 10 minutes delivers the desired local concentration (therapeutic window 25-1000 mg/L) for 3 days. Longer impregnation time at this concentration had no effect. Osteomycin® delivered the desired local concentration for 8 days in our experimental setting.

ABSTRACT 4

ABSTRACT 4

In vitro release of vancomycin from solution-impregna- ted bone chips and osteomycin® bonechips quantified using uplc-dad chromatography

Vancomycin-impregnated bonechips from a human morselized femoral head allograft (BCs) are used in orthopaedic surgery to treat infections. Literature suggests that bonechips can be efficient vancomycin carriers, but due to the diversity in the type of bonechips, of impregnation and of method used to evaluate AB release, there are no uniform guidelines. We performed an in vitro study to examine the release of vancomycin from solution-impregnated deep-frozen processed bonechips. Quantification was performed using a fully validated chromatographic method. Results were compared with the elution profile from Osteomycin®, a commercially available lyophilized processed bonegraft. Different vancomycin impregnation-concentrations and impregnation-durations of frozen processed bonechips were investigated. After impregnation, bonechips were rinsed with saline in order to determine only the absorbed vancomycin. Elution was performed in newborn calf serum at 37°C. Eluted vancomycin concentrations were determined using Ultra Performance Liquid Chromatography – Diode Array Detection (UPLC-DAD). In addition an elution study was performed on the commercially available Osteomycin®, bonechips containing vancomycin. Using processed frozen bonechips, an impregnation-concentration of minimum 100 mg/mL during 10 minutes delivers the desired local concentration (therapeutic window 25-1000 mg/L) for 3 days. Longer impregnation time at this concentration had no effect. Osteomycin® delivers the desired local concentration for 8 days in our experimental setting.

Literature suggests that fresh-frozen BCs can be used as carrier for vancomycin through solution-impregnation. There is however much less information on the carrier-capacities of frozen processed bonechips, a type used in our hospital. Our impregnation protocol was based on that of Mathysen et al., but with direct quantification of elution concentrations. Impregnation with vancomycin 100 mg/mL during 10 minutes results in a release above the desired concentration for 3 days, which seems too short when treating bone infections. Osteomycin® delivers the desired local concentration for 8 days in our experimental setting.

Vancomycin-solution impregnation of frozen processed bonechips may not be sufficient to obtain the desired release characteristics for the treatment of bone infections.
ARTIKELS

ABSTRACT 1
The occurrence of depersonalization symptoms after accelerated HF-RTMS of the left DLPFC: a case report

Geerts P., Lennens G., Baeken C.

With great interest we have read the recently published article of Jay and colleagues on single low frequency repetitive transcranial magnetic stimulation (LF-rTMS) applied to the right ventrolateral prefrontal cortex (VLPFC) in the treatment of depersonalization disorder [1]. Hereby supporting the hypothesis that inhibition of the right VLPFC increases autonomic activity and is able to reduce depersonalization symptoms. However, we report the occurrence of acute and severe depersonalization symptoms in a patient with chronic treatment-resistant major depression (TRD) treated with accelerated high frequency rTMS (HF/rTMS), applied to the left dorsolateral prefrontal cortex (DLPFC).

RESULTS
550 psychiatrist and emergency physicians were invited. The overall response rate was 20% (n = 108). The number 1 preferred medication classes were antipsychotics (59.3%) and benzodiazepines (40.7%). In non-secluded patients, olanzapine (22.2%), lorazepam (21.3%) and clozapine (19.4%) were most frequently picked as number 1 choice drug. In secluded patients, clozapine (22.3%) lorazepam (21.3%) and droperidol (14.8%) were the three most frequently chosen number 1 preferred drugs. Between-group comparisons show that emergency physicians prefer benzodiazepines significantly more than psychiatrists do. Zuclopenthixol and olanzapine show a particular profile in secluded patients. Benzodiazepines were significantly preferred over antipsychotics in secluded patients (P = 0.008). Safety or outcome monitoring are rarely used.

CONCLUSIONS
Our results show that prescription practice in Flanders (Belgium) in acute agitation shows a complex relationship with published guidelines. Prescription preferences differ accordingly to medical specialty. These findings should be taken into account in future research.

ABSTRACT 2
Prescribing preferences in rapid tranquillisation: a survey in Belgian psychiatrists and emergency physicians

Bervoets C., Bovill E., De Fruyt E., Demunter H., Dekeyser B., Vandenbussche L., Titeca K., Pieters G., Sabbe B., Roelant E., De Fruyt J., Demunter H., Dekeyser B., Merrey M.
BMC Res Notes. 2015;8:218.

BACKGROUND
The pharmacotherapeutic management of agitation is a common clinical challenge. Pharmacotherapy is frequently used, the use of published guidelines is not known. The purpose of this study was twofold: to describe the prescribing patterns of psychiatrists and emergency physicians and to evaluate to which extent guidelines are used.

METHODS
A cross-sectional survey in the Dutch-speaking part of Belgium is carried out in 39 psychiatric hospitals, 11 psychiatric wards of a general hospital and 61 emergency departments. All physicians are asked for demographic information, their prescribing preferences, their use of guidelines and the type of monitoring (effectiveness, safety). For the basic demographic data and prescription preferences descriptive statistics are given. For comparing prescribing preferences of the drug between groups Chi square tests (or in case of low numbers Fisher’s exact test) were performed. Mc Nemar test for binomial proportions for matched-pair data was performed to see if the prescription preferences of the participants differ between secluded and non-secluded patients.

RESULTS
Our results show that prescription practice in Flanders (Belgium) in acute agitation shows a complex relationship with published guidelines. Prescription preferences differ accordingly to medical specialty. These findings should be taken into account in future research.
ARTIKELS

ABSTRACT 1
Ostesitis pubis after TURP: a rare complication difficult to recognize
TURP is a widespread urologic procedure that is performed by many urologists. This report describes a rare complication that causes serious morbidity because it is not recognized in time. This is also the first report of a prostatosymphyseal fistula treated without major surgery. Eventually diagnosis is made by a MRI 5 months after surgery. Decompressive surgery was necessary to treat public osteesis with invalidating pain. Culture results revealed Escherichia coli but eventually the diagnosis was made by fistulography. Treatment consisted of bladder drainage and long-term antibiotic treatment and these could eventually heal the fistula.

ABSTRACT 2
Long-term efficacy and safety of enzalutamide monotherapy in hormone-naïve prostate cancer: 1- and 2-year open-label follow-up results
BACKGROUND
Enzalutamide is an androgen receptor inhibitor with demonstrated overall survival benefit in metastatic castration-resistant prostate cancer. A phase 2 study of enzalutamide monotherapy in patients with hormone-naïve prostate cancer (HNPC) showed a high response rate at week 25, (59%) presented with metastases at study entry. Of 67 patients enrolled, 45 (67%) remained on enzalutamide at week 97. For patients remaining on therapy, the PSA response rate at week 97 was 100% (95% confidence interval 92-100%). Of 26 patients with metastases at baseline, 13 (50%) had a complete and four (15%) had a partial response as best overall tumor response up to 97 wk on treatment. There was overall maintenance of total-body bone mineral density (BMD) and moderate changes in lean and fat body mass at 97 wk. The most common adverse events were gynecomastia, nipple pain, fatigue, and hot flushes. The study limitations include lack of a control group and of endocrine, glycemic, and lipid data at 97 wk.

CONCLUSIONS
Long-term enzalutamide monotherapy in men with non-castrate HNPC is associated with large sustained reductions in PSA, signals indicating a favorable tumor response, and favorable safety/tolerability profile, with relatively small negative effects on total-body BMD.

ABSTRACT 3
Editorial comment to current use of active surveillance for localized prostate cancer: a nationwide survey in Japan
Active surveillance (AS) is now firmly established as the preferred management strategy for many men with low-risk prostate cancer. Even in the USA where AS has traditionally been underutilized, urologists have now started to embrace AS, while in Australia, AS is used as the primary management strategy for 37% of men with low-risk disease and 8.9% of men with intermediate-risk disease. For low-risk disease, several large AS studies show this to be a safe and feasible management option with mature data showing 10- and 15-year actuarial cause-specific survival rates of 98.1% and 94.3%, respectively. At 5- and 10-year follow up, 75.7% and 63.5% remain intervention-free, thereby avoiding the undoubted morbidity of surgery or radiation therapy. All of the major guidelines have now endorsed this strategy, which certainly goes some way to addressing the issue of overtreatment in the screen-detected population of patients who have emerged with the widespread use of prostate-specific antigen testing in recent years. What then are we to make of this interesting pattern of care paper published in the International Journal of Urology this month? In this large survey of 1633 urologists, we get the first real sense of the use of AS in Japan and of the attitudes of Japanese urologists towards AS. There are a few interesting observations. First, it seems remarkable that over one-quarter (26.2%) of urologists had "no use for AS," despite the convincing evidence and guideline recommendations for the safety of AS for low-risk disease. While accepting that most published studies are in non-Japanese populations, this high rate of disapproval of AS does seem to represent a remarkably negative view of AS in general. Second, the lack of standardization in the use of AS protocols is noteworthy, especially as the majority of respondents do not routinely use repeat prostate biopsies as part of the follow up for men on AS. Overall, 40.1% of respondents carried out repeat biopsy at 1 year (in line with published protocols), but 24.1% “did not usually” carry out repeat biopsy and 31.8% carried it out “only when they consider it necessary.” All of those who did use a standardized protocol, the Prostate Cancer Research International Active Surveillance (RIAS) study was most frequently used. Magnetic resonance imaging scanning was used in up to 90% of respondents at the time of initiation of AS, and it was noted that older urologists were less likely to use AS. It was also remarked by the authors that some respondents did not discriminate between AS and watchful waiting when presented with a case of an older patient with multiple comorbidities. This study provides an interesting contemporary overview of AS in Japan. It is encouraging that knowledge and use of AS is high in many centers, but there also is some negativity and variability in how AS is being practiced. It would be helpful to see protocols (such as Prostate Cancer Research International Active Surveillance or the Multiple Japan AS study) being more widely encouraged.

ABSTRACT 4
Porcine cadaver organ or virtual-reality simulation training for laparoscopic cholecystectomy: a randomized, controlled trial
OBJECTIVES
As conventional laparoscopic procedural training requires live animals or cadaver organs, virtual simulation seems an attractive alternative. Therefore, we compared the transfer of training for the laparoscopic cholecystectomy from porcine cadaver organs vs virtual simulation to surgery in a live animal model in a prospective randomized trial.

DESIGN
After completing an intensive training in basic laparoscopic skills, 3 groups of 10 participants preceded with no additional training (control group), 5 hours of cholecystectomy training on cadaver organs (= organ training) or proficiency-based cholecystectomy training on the Lap-Mentor (= virtual-reality training). Participants were evaluated on time and quality during a laparoscopic cholecystectomy on a live anaesthetized pig at baseline (= week 0), = week 1 (post) and 4 months (= retention) after training.

SETTING
All research was performed in the Center for Surgical Technologies, Leuven, Belgium.

PARTICIPANTS
In total, 30 volunteering medical students without prior experience in laparoscopy or minimally invasive surgery from the University of Leuven (Belgium).

RESULTS
The organ training group performed the procedure significantly faster than the virtual trainer and borderline significantly faster than control group at posttesting. Only 1 of 3 expert raters suggested significantly better quality of performance of the organ training group compared with both the other groups at posttesting (p < 0.03). There were no significant differences between groups at retention testing. The virtual trainer group did not outperform the control group at any time.

REFERENCE
CONCLUSIONS
For trainees who are proficient in basic laparoscopic skills, the long-term advantage of additional procedural training, especially on a virtual but also on the conventional organ training modal, remains to be proven.

ABSTRACT 5
The use of sling vs sphincter in post-prostatectomy urinary incontinence
Van Brusselaene S., De Ridder D., Van der Aa F.
BJU Int. 2015;116(3):330-342.
The artificial urinary sphincter (AUS) is considered the ‘gold standard’ in post-prostatectomy urinary incontinence. However, in recent years, male slings have gained much popularity due to the ease of surgery, good functional results and low complications rates. This review systematically shows the evidence for the different sling systems, describes the working mechanism, and compares their efficacy against that of the AUS. Furthermore, subgroups of patients are defined who are not suited to undergo sling surgery.

ABSTRACT 6
Surgical skill trick or trait?
OBJECTIVE
Among other indispensable qualities, a competent surgeon needs to be technically skilled. With the advent of minimal invasive procedures, technical demands on surgeons also increase. Will it be possible for all individuals to meet these technical demands through motivated practice or is there a trait such as “aptitude” that determines ultimate surgical skill?

DESIGN
Baseline laparoscopic psychomotor aptitude (on a box trainer), visual-spatial aptitude (Schulz figures test), and interest in surgery (10-point Likert scale) were assessed prior to laparoscopic psychomotor aptitude, eventually students with high aptitude do not automatically train more. No correlation was found between aptitude and amount of voluntary practice. High-aptitude students more frequently applied for surgical disciplines in their final career choice (50% vs 18%, p < 0.01).

RESULTS
Multiple additive regression analysis showed significant effect for psychomotor aptitude (26%), interest in surgery (9%), and voluntary practice (18%) on final box trainer performance. No correlation was found between aptitude and interest in surgery (p < 0.27). No correlation was found between aptitude and amount of voluntary practice. High-aptitude students more frequently applied for surgical disciplines in their final career choice (50% vs 18%, p < 0.01).

CONCLUSIONS
This study shows that aptitude and motivated practice equally influence final box trainer performance. Students with lower aptitude do not automatically train more. Although the interest in surgery was initially not related to psychomotor aptitude, eventually students with high aptitude apply more frequently for a surgical career.

Followed by 2 additional weeks of voluntary practice for those who were motivated to do so. After these 2 weeks, participants were retested using the laparoscopic box trainer.

SETTING
All research was performed in the Center for Surgical Technology, Leuven.

PARTICIPANTS
A total of 65 fifth-year medical students without prior experience in laparoscopy from the University of Leuven.

RESULTS
Principal outcomes measured were prostate-specific antigen (PSA) response (defined as a decrease ≥ 50%), time to PSA progression (defined as an increase ≥ 50% over PSA nadir in case of PSA response or > 25% in the absence of PSA response), time to radiographic progression (according to Response Evaluation Criteria in Solid Tumors 1.1 criteria), overall and cancer-specific survival and occurrence of adverse events (according to Common Terminology Criteria for Adverse Events v4.03). Kaplan-Meier statistics were applied.

RESULTS
A PSA response ≥ 50% was observed in 121 patients (37%). Median time to PSA progression was 4.1 months [95% confidence interval (CI) 3.6 to 4.6]. Median time to radiographic progression was 5.8 months [95% CI 5.3 to 6.4]. Median overall and cancer-specific survival was 15.1 months [95% CI 13.6 to 16.6] and 16.8 months [95% CI 14.6 to 19.0] respectively. The most common grade 3-4 adverse events were anaemia (33.9%), hypokalaemia (7.1%), fatigue (6.9%) and pain (6.9%). Median duration of AA treatment was 5.3 months [interquartile range 2.8 to 10.3 months].

CONCLUSIONS
This real-world data on AA efficacy is in line with data from the AA phase III trial post-docetaxel. Importantly, incidence of anaemia and hypokalaemia is about 50% higher than reported in previous studies.

ABSTRACT 1
Evaluation of abiraterone acetate post-docetaxel in the Belgian compassionate use program
American Society of Clinical Oncology Annual Meeting – May 2015 (Chicago, USA)

ABSTRACT 2
Phase 3, randomized, double-blind, placebo-controlled study of tasquinimod (TASQ) in men with metastatic castrate-resistant prostate cancer (mCRPC)
European Cancer Congress – September 2015 (Vienna, Austria)

BACKGROUND
TASQ is a novel oral immunotherapy with immunomodulatory, anti-angiogenic and anti-metastatic properties; it targets the tumor microenvironment by binding to S100A8 and modulating regulatory myeloid cells. In a randomized phase 2 trial in men with mCRPC (NC- T00564082), TASQ increased PFS and showed a trend to an OS benefit in chemotherapy-naïve patients (pts) vs placebo (PBO) (Pili et al. JCO 2011;29:4022) This is a phase 3 study (NCT01234311) conducted to confirm the phase 2 findings.

MATERIAL AND METHODS
Men with asymptomatic to mildly symptomatic chemother-apy-naïve mCRPC; and evidence of os metastases were assigned (2:1) to receive TASQ once daily (initial dose 0.25mg [ escalation to 1.0mg/d or 4 wks [or maximum tolerated dose]) or PBO until progression or toxicity. Randomization was stratified by KPS (<90% vs ≥90%), presence/absence of visceral disease, and geographic region. The primary endpoint was radiographic PFS (rPFS) per Prostate Cancer Working Group 2 criteria and RECIST 1.1. Planned sample size was 1200 pts to achieve 99.9% power to detect a rPFS hazard ratio (HR) of 0.6 with a 2-sided alpha error of 0.05. The trial had 80% power to detect a target HR of 0.8 for OS, a key secondary endpoint. Other secondary endpoints included additional clinical outcome measures and safety. Data are presented from the final analysis on 13 Feb 2015 after a minimum of 727 OS events (6 Dec 2013 for rPFS).

RESULTS
1245 pts were randomized (TASQ, n=832; PBO, n=413) between 29 Mar 2011 and 7 Dec 2012 at 240 sites in 27 countries. 2 baseline characteristics were balanced between the 2 groups: median age: 73 years; KPS ≥90%: 77.3%; presence of visceral metastasis: 21.1%.

PRESENTATIES CONGRESSEN

ABSTRACT 1
Evaluation of abiraterone acetate post-docetaxel in the Belgian compassionate use program
American Society of Clinical Oncology Annual Meeting – May 2015 (Chicago, USA)

ABSTRACT 2
Phase 3, randomized, double-blind, placebo-controlled study of tasquinimod (TASQ) in men with metastatic castrate-resistant prostate cancer (mCRPC)
European Cancer Congress – September 2015 (Vienna, Austria)
Estimated median rPFS by central review was 7.0 mo (95% CI 5.9–9.2) with TASQ and 4.4 mo (95% CI 3.5–5.5) with PBO (HR 0.639 [95% CI 0.544–0.751]; p<0.001). For rPFS by local review, estimated median was 5.7 mo (95% CI 5.5–6.2) with TASQ and 4.1 mo (95% CI 3.1–5.1) with PBO (HR 0.693 [95% CI 0.599–0.803]; p<0.001). With a median follow-up of 30.0 mo for TASQ and 30.7 mo for PBO, median OS was 21.3 mo (95% CI 19.5–23.0) with TASQ and 24.0 mo (95% CI 21.4–26.0) with PBO (HR 1.097 [95% CI 0.938–1.282]; p=0.247).

Other secondary efficacy endpoints: median time to KPS deterioration ≥20% was 11.7 mo for TASQ and 17.4 mo for PBO (HR 1.3 [95% CI 1.11–1.50]; p<0.001) and time to initiation of further anticancer therapy was 11.4 mo for TASQ vs 8.1 mo for PBO (HR 0.78 [95% CI 0.67–0.91]; p=0.001). Grade ≥3 TEAEs were more frequent with TASQ than PBO (42.8 vs 33.6%). TEAEs leading to death were 3.3% with TASQ and 3.6% with PBO.

CONCLUSIONS
In chemotherapy-naïve men with mCRPC, single-agent TASQ statistically significantly improved rPFS, by both central and local review, as compared to PBO. No OS benefit was observed with TASQ.