



### Science Meeting – Scientific Report

***Proposal Title:*** 12<sup>th</sup> Scientific Meeting of the European Network for the Study of Adrenal Tumours (ENSAT) – 22<sup>nd</sup>-23<sup>rd</sup> November, Budapest, Hungary

***Application Reference N°:*** 5116

***Local organizer:*** Dr. Peter Igaz MD PhD DSc, Steering Committee member of the Hungarian Society of Endocrinology and Metabolism  
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#### 1) Summary (up to one page)

The 12<sup>th</sup> Scientific Meeting of the European Network for the Study of Adrenal Tumours (ENSAT) was held in Budapest, Hungary at the Danubius Hotel Health Spa Resort Helia. This has been the first time that the meeting took place in Central-Eastern Europe.

The scientific programme of the meeting has been established by the ENSAT Steering Committee (Felix Beuschlein, Wiebke Arlt, Henri Timmers, Massimo Terzolo, Anne-Paule Gimenez-Roqueplo, Jerome Bertherat) and the heads of the four working groups of ENSAT (Martin Fassnacht, Maria-Christina Zennaro, Massimo Terzolo and Anne-Paule Gimenez-Roqueplo) along with the local organizer Peter Igaz.

The scientific programme was divided according to the major interests of ENSAT (adrenocortical cancer (ACC), pheochromocytoma/paraganglioma (PHEO/PGL), aldosterone producing adenoma (APA), non-aldosterone producing adenoma (NAPACA)). ENSAT is a European collaborative network aimed at the promotion of research in the fields of adrenal tumour pathogenesis, diagnosis and therapy. All of these topics have been covered in the discussions and presentations.

The meeting in Budapest has been so far the largest scientific meeting of ENSAT with 142 registered participants from 17 countries (France, Germany, Italy, UK, the Netherlands, Hungary, Spain, Norway, Sweden, Bulgaria, Russia, USA, Brazil, Australia, Croatia, Poland, Greece).

77 abstracts have been submitted and accepted. 32 short oral communications and 45 posters have been presented.

The first day of this two day meeting has been dedicated to working group sessions. Two of these have run in parallel (ACC and APA, PHEO/PGL and NAPACA). General Assembly (including the presentation on ENSAT registry by A. Stell) and the presentation of novel projects closed the first day, whereas short oral communications and posters have been presented during the second day of the meeting.

## 2) Description of the scientific content of and discussions at the event (up to four pages)

Intensive discussion of ongoing and future research projects has taken place during the working group meetings on Friday afternoon (22<sup>nd</sup> November: ACC and APA in parallel followed by PHEO/PGL and NAPACA in parallel).

In the ACC WG session several ongoing projects have been presented including the tissue microarray project (T. Papathomas), the ENSAT-Cancer OMICS and TCGA projects (J. Bertherat and M. Fassnacht), and the standardization of Ki67 immunohistochemistry (T. Papathomas). The session began with a short update on the ENSAT Database by A. Stell that is developing rapidly and involves more than 1800 patients at present. Further studies including circulating microRNAs, hair mitotane measurement, EURINE-ACT by W. Arlt (Birmingham) and ADIUVO by M. Terzolo (Turin). During the APA WG session two ongoing projects by GP Rossi have been presented (The Adrenal Vein Sampling International Study (AVIS) For Identifying the Major Subtypes of Primary Aldosteronism; PAPPHY (Prospective Appraisal of the Prevalence of Primary Aldosteronism in HYPertensive patients presenting with atrial flutter or fibrillation). The PHEO WG session included reports of the ongoing projects (Srirangalingam Umasuthan: Clinical Endocrine Audit Proposal - Management of subjects in the UK with pheochromocytomas or paragangliomas, Eric Baudin : PMM progno study, Mariko Sue: the PMT3 study).

The 77 submitted abstracts covered numerous topics in the fields of tumourigenesis, diagnosis and therapy of both adrenocortical and adrenomedullary tumours.)

Oral communications and posters have been ordered following the tumourigenesis-diagnosis-therapy axis. This meeting has been the first among ENSAT meetings, where guided poster tours (parallel for ACC, PHEO/PGL and APA+NAPACA) have been organized. Moreover, four poster prizes representing the four working groups of ENSAT have been offered and awarded to first authors under 35 years of age.

Below, we present the most relevant findings presented:

### **Adrenocortical cancer (ACC):**

- i. *Ruggiero et al.* from E. Lalli's group (Nice) demonstrated that increased steroidogenic factor 1 (SF-1) expression might promote invasiveness and metastatic potential of adrenocortical cells (OR01 – oral communication).

- ii. *Lefevre et al.* showed the involvement of AFF3 (AF4/FMR2 family, member 3) in the Wnt/ $\beta$ -catenin pathway, and this might represent a novel and important player in adrenocortical tumourigenesis (OR01 – oral communication).
- iii. *Ronchi et al.* from Wuerzburg revealed that high CYP2W1 expression might represent a new prognostic factor in ACC, as it was found to be associated with a better disease free survival in early tumor stages (OR03 - oral communication).
- iv. *Latre de Laté et al.* (Nice) reported the relevance of the Vanin-1 gene in adrenocortical tumourigenesis based on elegant experiments performed on SF-1 transgenic mice (OR-04 – oral communication).
- v. *Duregon et al.* (Turin) showed that Phosphohistone H3 Ser 10 (PHH3) staining could be a useful marker for assessing tumour proliferation as a complimentary tool mostly in ACC with low mitotic counts, and Ki-67 staining is the best method for measuring tumour proliferation (OR-05 – oral communication).
- vi. In the OR06 oral communication presented by *P. Igaz* (Budapest), the results of plasma microRNA profiling in adrenocortical tumours have been presented. Five microRNAs have been found that showed differential expression (overexpression in ACC) that might be later used even as minimally invasive markers of malignancy. Several technical problems associated with the study of plasma microRNAs have been discussed.
- vii. In one of the most significant studies presented, *Jouinot et al.* from J. Bertherat's group (Paris) presented the relevance of methylation that can be used for prognosis stratification and tumour classification (OR07 - oral communication).
- viii. A potential novel therapeutical option has been discussed by *Hantel et al.* from Felix Beuschlein's group (Munich) involving TNF $\alpha$  and Toll-like-receptor 4–signalling by Tumor-Vascular-Disrupting Agent ASA404 (vadimezan). (OR08 – oral communication)
- ix. *Sbiera et al.* from Wuerzburg presented a novel way of action of mitotane (the only adrenal-specific drug for ACC at present with only partly understood mechanism of action) involving endoplasmic reticulum stress and reduced apoptosis (OR09-oral communication).
- x. In the other presentation by *P. Igaz* (Budapest, OR10), the in vitro and in vivo activity of 9-cis retinoic acid has been discussed that might represent a potentially novel treatment option in ACC.
- xi. Thalidomide is not an encouraging option for ACC treatment (OR11)
- xii. *Kerkhofs et al.* from H. Haak's group (Eindhoven) presented an interesting pharmacokinetic model of mitotane that can be exploited in the clinical management of patients treated (OR12).

- xiii. EGFR mutation status assessment might be useful in a subset of ACC patients (P2 by *Wikander et al.*).
- xiv. Overexpression of the EZHZ histone methyltransferase might be relevant for ACC progression (P4 by *Drelon et al.*).
- xv. The poster award has been won by *C. Hantel et al.* from F. Beuschlein group (Munich) reporting the establishment of patient individual tumour models for endocrine tumours (P8).
- xvi. The laterality difference between ACC and PHEO has been presented by *Bala et al.* (P9) from M. Fassnacht's group. This study also serves as a basis for a future project on laterality involving all working groups.

### **Benign adrenocortical adenomas (APA + NAPACA)**

- i. There have been several reports on the relevance of somatic mutations in aldosterone producing adenomas (ATP1A1, ATP2B3 and KCNJ5 by *Williams et al.*, OR13; KCNJ5, CACNA1D, ATP1A and ATP2B3 by *Fernandez-Rosa et al.* from MC Zennaro's group – OR14, ATP1A1 and ATP2B3 by *Akerström et al.* – OR15, *Nyirő et al.* – P36).
- ii. *L. Amar et al.* from S. Boulkroun's group reported the use of immunohistochemical analysis for discrimination of aldosterone-producing adenomas from other tumours and to predict its mutation status – OR16. This might represent a major finding also from a practical point of view.
- iii. The cardiovascular complications of primary aldosteronism have been discussed by *Savard et al.* reporting a cross-sectional study (OR18) and by *P. Mulatero et al.* along with the cerebrovascular complications (OR19).
- iv. The poster prize was won by *Mirko Peitsch* (P38) from Dresden for a study on LC-MS/MS based steroid profiling in adrenal venous samples.

### ***Fewer reports have been discussing the field of non-aldosterone producing adrenal tumours (NAPACA).***

- v. In M. Doleschalls's presentation (Budapest), the different ACTH-induced hormone levels in relation to 21-hydroxylase (CYP21A2 gene) haplotypes (OR20).
- vi. In another presentation by E. Lalli's group, *M. Doghman* discussed the relevance of SF1 transcription factor dosage impact on genome-wide binding and gene expression regulation (OR21).
- vii. The relevance of glucocorticoid receptor polymorphisms have been discussed in incidentalomas by *G. Reimondo et al.* from M. Terzolo's group (Turin) (OR22) and in hormonally inactive adrenal tumours by *Acs et al.* (Budapest) (P39).

- viii. The poster prize in the NAPACA category was awarded to *Barbara Altieri* (P41) for a detailed immunohistochemical analysis of adrenocortical tumours.

### **Phaeochromocytoma/paraganglioma**

- i. *J. Favier* from Paris presented a hot topic in PHEO research regarding the association of SDH gene mutations with a hypermethylator phenotype (OR23). This study has been published in *Cancer Cell*.
- ii. Promoter mutations of the telomerase reverse transcriptase (TERT) have been discussed by *T. Papathomas et al.* from Eindhoven both in extra-adrenal PGL and ACC (OR24).
- iii. Results of a large collaborative study have been presented by *J. Dénes et al.* from M. Korbonits's group (London) on the heterogeneous genetic background of pituitary tumours associating with PHEO/PGL (OR25).
- iv. The molecular pathogenesis of PHEO have been discussed in several studies including the relevance of MAX and hypoxia inducible factors (*Qin et al.* from G. Eisenhofer's group Dresden (OR26)), BMP7 by *Repokis et al.* (OR27).
- v. *Anne-Paule Gimenez-Roqueplo* from Paris has presented major findings of germline and somatic mosaicism in HIF2 $\alpha$ -related polycythaemia-paraganglioma syndrome (OR28).
- vi. *L. Amar* from Paris discussed a rare clinical syndrome related to PHEO/PGL, acute catecholamine cardiomyopathy that can pose major differential diagnostic problems in the management of acute patients (OR29).
- vii. In the communication by *van Berkel et al.* (OR30) from H. Timmers's group, the association of <sup>18</sup>F-DG-PET with immunohistochemical parameters of glycolysis has been examined.
- viii. The seasonal changes in catecholamine metabolite levels reported by *Pamporaki et al.* (OR31) from G. Eisenhofer's group could have major clinical relevance in the diagnosis of PHEO/PGL.
- ix. The poster prize in this category has been awarded to *Christian Ziegler* (P17) who developed a novel fluorescence-based animal model for PHEO.
- x. *Fliedner et al.* from NIH reported the potential anticancer potential of MAPK inhibitors in PHEO (P18).
- xi. *Dematti et al.* from G. Opocher's group analyzed the prevalence of pituitary tumours in the Trentino region where a high prevalence of SDH mutation carriers has been reported. The prevalence of pituitary adenoma was 11.7% with macroadenomas occurring in 3%,

**3) Assessment of the results and impact of the event on the future directions of the field (up to two pages)**

The 12<sup>th</sup> Scientific Meeting of ENS@T was a very active and intensive meeting that enabled the leading researchers in the field of adrenal tumours to perform fruitful discussions. Several major results have been presented (e.g. the relevance of methylation in both adrenocortical and adrenomedullary tumours (Jouinot et al., Letouzé et al.), new therapeutical options and diagnostic tools, as well.

The following novel projects have been proposed during the meeting that will serve as basis for future collaboration within the ENS@T framework:

- i- SuMit trial - sunitinib vs. mitotane as first-line therapy in advanced ACC (Matthias Kroiss, Wuerzburg).
- ii- Phase I FGF-R inhibitor BAY1163877 (Matthias Kroiss, Wuerzburg)
- iii- Initiation of a “Surgical working group” (Sébastien Gaujoux, Paris – this might represent a novel aspect in ENS@T, as surgeons have been underrepresented to date).
- iv- Assessment of heterogeneity in surgical procedures, operative notes and pathological report (Sébastien Gaujoux, Paris)
- v- Laterality of adrenal tumors (Martin Fassnacht, Margarita Bala, Wuerzburg) – this project is a simple, but very promising project. It seems that ACC is more frequent on the left, whereas PHEO on the right side. This could be easily examined by using the ENSAT database for all tumours. This study seems to be of interest for all working groups.
- vi- Recurrence-frequency after 5-year relapse-free survival by ACC-patients (Martin Fassnacht, Wuerzburg)
- vii- Prospective Validation of Individualized Mitotane Dosing Using Pharmacokinetic Modeling (PROVIM) (Harm Haak, Eindhoven)
- viii- How long to treat with mitotane in the adjuvant setting? (Massimo Terzolo, Turin, Martin Fassnacht, Munich)
- ix- Development of ovarian cysts in women of childbearing age treated adjuvantly with mitotane (Massimo Terzolo, Turin)
- x- Retrospective analysis of patients treated with gemcitabine + capecitabine after failing EDP-M (Matthias Kroiss, Martin Fassnacht Wuerzburg, Alfredo Berruti, Brescia)
- xi- Primary aldosteronism and pregnancy (a retrospective multicentric study involving several ENSAT centres with the primary objective to define the

- prevalence of preeclampsia and identification of prognosis factors) (Laurence Amar, Paris)
- xii- HNO-study: prospective head neck paraganglioma study (Christina Pamporaki, Dresden)
- xiii- Non-conventional imaging methods in diagnosis of PHEO-PGL (Anna A Kasperlik-Zaluska, Poland)
- xiv- Mediastinal PGL (Laurence Amar, Paris)
- xv- : NGS and EEQ for the genetic testing of PCC/PGL (Anne-Paule Gimenez-Roqueplo, Paris)

The meeting has been considered to be successful by most participants. With the largest number of attendees so far during ENS@T Scientific Meetings, the ENS@T network is growing. Numerous novel projects have been proposed that show the activity of the network.

International collaborative networks are of pivotal importance for the study of rare diseases (including several forms of adrenal tumours) and the ENS@T network is an outstanding project with already significant achievements that are expected to continue in the future.

The next 13<sup>th</sup> Scientific meeting of ENSAT will be held on 21-22. November 2014. in Nice (France) hosted by Dr. Enzo Lalli.

**We would like to thank the European Science Foundation (ESF-ENSAT) for supporting our meeting. Support from ESF-ENSAT was invaluable for the successful organisation of the meeting.**

Budapest, 9. December 2013.



Dr. Peter Igaz MD PhD DSc  
Local organiser

**4) Annexes 4a) and 4b): Programme of the meeting and full list of speakers and participants**

**Annex 4a: Programme of the meeting**

**Annex 4b: Full list of speakers and participants**

**Final programme of the 12<sup>th</sup> Scientific Meeting of the European Network for the Study of Adrenal Tumours (ENS@T) in Budapest 22-23. November 2013.**

**22. November, Friday**

*13.00-14.00 Lunch*

**14.00-14.10 Welcome address (Peter Igaz, Felix Beuschlein) Ball Room**

**14.10-18.00 Working Group meetings:**

**14.10-16.00. Adrenocortical cancer (ACC) Working Group (Ball Room) –  
*Martin Fassnacht***

**14.10-16.00. Pheochromocytoma Working Group (Panorama Room) –  
*Anne-Paule Gimenez-Roqueplo***

*Coffee Break 16.00-16.20*

**16.20-18.00 NAPACA Working Group (Ball Room) – *Massimo Terzolo***

**16.20-18.00 Aldosterone producing adenoma APA Working Group (Panorama Room) –  
*Maria-Christina Zennaro***

**18.00-18.30 General assembly** (20 Minutes + 10 Minutes registry presentation by Anthony Stell) (Ball Room)

**18.30-19.30. Presentation of Project proposals** (e.g. 5 minutes each including discussion, chaired by the Working Group heads) (Ball Room)

*20.30- Dinner at the Hotel*

**23. November, Saturday**

**8.00-10:00. 12 oral presentations (7 minutes + 3 minutes discussion) on Adrenocortical Cancer (ACC) (Ball Room)**

***Chairs: Eric Baudin and Michaela Luconi***

**OR01 8.00-8.10**

**Increased Steroidogenic factor-1 dosage promotes Rho small GTPase activation, actin cytoskeleton remodelling and invasion of human adrenocortical cancer cells**

Ruggiero C, Doghman M, Lalli E



**OR02 8.10-8.20**

**AFF3, a new target of Wnt/ $\beta$ -catenin pathway, involved in adrenocortical carcinoma**

Lucile Lefevre, Hanin Omeiri, Ludivine Drougat, Stéphanie Rodriguez, Karine Perlemoine, Marthe Rizk-Rabin, Jérôme Bertherat, Bruno Ragazzon

**OR03 8.20-8.30**

**Expression of CYP2W1 in adrenal gland: relationship with hormone secretion and tumor development**

Cristina L. Ronchi, Silviu Sbiera, Marco Volante, Sonja Steinhauer, Vanessa Wild, , Massimo Terzolo, Martin Fassnacht, Bruno Allolio

**OR04 8.30-8.40**

**Role of the VANIN-1 gene in adrenocortical tumorigenesis in mice**

Perle Latré de Laté, Abeer El Wakil, Marielle Jarjat, Philippe Naquet, Tanya Karpova, Leslie L. Heckert, Enzo Lalli

**OR05 8.40-8.50**

**Diagnostic and prognostic role of morphological and phospho-histone H3-based mitotic count compared to Ki-67 proliferation index in adrenocortical carcinoma**

Eleonora Duregon, Luca Molinaro, Marco Volante, Laura Ventura, Luisella Righi, Stefania Bolla, Massimo Terzolo, Anna Sapino, Mauro Papotti

**OR06 8.50-9.00**

**Plasma microRNAs in adrenocortical tumours**

Diana Rita Szabó, Michaela Luconi, Peter M. Szabó, Miklós Tóth, Nikolette Szücs, János Horányi, Zoltán Nagy, Massimo Mannelli, Attila Patócs, Károly Rácz, Peter Igaz

**OR07 9.00-9.10**

**Development of a prognostic tool of adrenocortical cancer (ACC) based on DNA methylation analysis**

Anne Jouinot, Guillaume Assié, Rossella Libé, Olivia Barreau, Thomas Papatomas, Nadim Hamzaoui, Silviu Sbiera, Christina Ronchi, Matthias Kroiss, Jens Waldmann, Marcus Quinkler, Felix Beuschlein, Massimo Mannelli, Michaela Luconi, Franco Mantero, Jonathan Grivel, Stephanie Rodriguez, Lionel Groussin, Eric Baudin, Xavier Bertagna, Eric Clouser, Ronald de Krijger, Martin Fassnacht, Jérôme Bertherat

**OR08 9.10-9.20**

**Differential TNF $\alpha$  and Toll-like-receptor 4–signaling in endocrine tumors after Tumor-Vascular-Disrupting Agent ASA404 (vadimezan) and TNF $\alpha$  treatment**

Constanze Hantel, Regia Lira, Alexandra Ozimek, Roman Frantsev, Martin Reincke, Thomas Mussack, Felix Beuschlein

**OR09 9.20-9.30**

**Mitotane induces endoplasmic reticulum stress triggering apoptosis and decrease of steroid hormone synthesis**

Silviu Sbiera, Laura Wiemer, Ellen Leich, Annemarie Gehl, Felix Gardill, Cristina L. Ronchi, Margarita Bala, Andreas Schirbel, Andreas Rosenwald, Bruno Allolio, Martin Fassnacht, Matthias Kroiss

**OR10 9.30-9.40**

**Antitumoral effects of 9-cis retinoic acid in adrenocortical cancer: in vitro and in vivo studies**

Diana Rita Szabó, Kornélia Baghy, Peter M. Szabó, Zoltán Nagy, Ilona Kovalszky, Attila Patócs, Károly Rácz, Peter Igaz

**OR11 9.40-9.50**

**Treatment of advanced adrenocortical carcinoma with thalidomide: discouraging results of a retrospective analysis of 14 patients**

Timo Deutschbein, Daniela Körbl, Christina L. Ronchi, Felix Beuschlein, Bruno Neu, Marcus Quinkler, Margarita Bala, Stefanie Hahner, Bruno Allolio, Martin Fassnacht, Matthias Kroiss, on behalf of the German Adrenocortical Carcinoma Study Group

**OR12 9.50-10.00**

**Developing a pharmacokinetic model of mitotane: towards personalized medicine in adrenocortical carcinoma**

Kerkhofs TMA, Derijks LJJ, Eттаieb MHT, Den Hartigh J, Neef C, Gelderblom AJ, Guchelaar HJ, Haak HR

*10:00-10:30 Coffee break*

**10:30-12:10. 10 oral presentations ((7 minutes + 3 minutes discussion)) on adrenocortical adenomas (7 APA + 3 NAPACA) (Ball Room)**

***Chairs: Martin Reincke and Olivier Chabre***

**OR13 10.30-10.40**

**Somatic ATP1A1, ATP2B3 and KCNJ5 mutations in aldosterone-producing adenomas**

Tracy Ann Williams, Silvia Monticone, Vivien R. Schack, Julia Stindl, Fabrizio Buffolo, Felix Beuschlein, Martin Reincke, Francesco Fallo, Giampaolo Bernini, Mauro Maccario, Gilberta Giacchetti, Franco Veglio, Richard Warth, Bente Vilsen, Paolo Mulatero

**OR14 10.40-10.50**

**Prevalence of KCNJ5, CACNA1D, ATP1A and ATP2B3 mutations in aldosterone producing adenoma**

Fabio Luiz Fernandes-Rosa, Benoit Samson-Couterie, Laurence Amar, Xavier Jeunemaitre, Sheerazed Boulkroun, Maria-Christina Zennaro

**OR15 10.50-11.00**

**Mutations in ATP1A1 and ATP2B3 in aldosterone producing adenomas**

Tobias Akerström, Kenko Cupisti, Julian Ip, Holger Sven Willenberg, Jan Zedenius, Ana Moser<sup>6</sup>, Hendrik Lehnert, K. Alexander Iwen, Bruce Robinson, Stan Sidhu, Martin Anlauf, Henning Dralle, Martin Bäckdahl, Gunnar Westin, Per Hellman, Peyman Björklund

**OR16 11.00-11.10**

**Immunohistological diagnosis of aldosterone producing adenoma and tumor mutation status**

Laurence Amar; Fabio Luis Fernandes-Rosa; Benoit Samson-Couterie; Frédérique Tissier; Jérôme Bertherat; Tchao Meatchi; Maria-Christina Zennaro; Sheerazed Boulkroun

**OR17 11.10-11.20**

**Lack of influence of somatic mutations on steroid gradients of adrenal vein sampling in aldosterone producing adenomas**

Osswald A, Fischer E, Degenhart C, Quinkler M, Bidlingmaier M, Pallauf A, Lang K, Mussack T, Hallfeldt K, Beuschlein F, Reincke M.

**OR18 11.20-11.30**

**Cardiovascular complications associated with primary aldosteronism: a controlled cross-sectional study**

Savard S, Amar L, Plouin PF, Steichen O

**OR19 11.30-11.40**

**Long-term Cardio- and Cerebro-Vascular Events in Patients with Primary Aldosteronism**

Paolo Mulatero, Silvia Monticone, Chiara Bertello, Andrea Viola, Davide Tizzani, Andrea Iannaccone, Valentina Crudo, Jacopo Burrello, Alberto Milan, Franco Rabbia, Franco Veglio

**OR20 11.40-11.50**

**Haplotypes of the steroid 21-hydroxylase gene (CYP21A2) are related to ACTH-induced steroid hormone levels**

Marton Doleschall, Julianna Anna Szabo, Juilia Pazmandi, Agnes Szilágyi, Klara Koncz, Miklos Toth, Zoltan Prohaszka, Edit Glaz, Karoly Racz, Attila Patocs

**OR21 11.50-12.00**

**Integrative analysis of SF-1 transcription factor dosage impact on genome-wide binding and gene expression regulation**

Mabrouka Doghman, Bonald C. Figueiredo, Marco Volante, Mauro Papotti, Enzo Lalli

**OR22 12.00-12.10**

**Analysis of BclI, N363S and ER22/23EK polymorphism of the glucocorticoid receptor gene in a large series of patients with adrenal incidentaloma.**

G. Reimondo, M. Coletta, D. Giachino, I. Chiodini, D. Kastelan, V. Morelli, S. Cannavi, A. Cuccurullo, P. Beck-Peccoz, M. De Marchi, M. Terzolo

*12.10-13.10 Lunch + ENSAT Steering Committee Meeting (Venus room)*

**13.10-14.30 Guided poster tours (3 minutes for presentation + 2 minutes discussion in 3 parallel sessions) + ESF-ENSAT Steering Committee Meeting (Venus room)**

1. 16 posters on ACC (P1-P16) *Chairs: Harm Haak and Enzo Lalli*

2. 15 posters on PHEO (P17-P31) *Chairs: Mercedes Robledo and Ronald de Krijger*

3. 14 posters on APA + NAPACA (P32-P45) *Chairs: Sheerazed Boulkroun and*

*Darko Kastelan*

**14.30-16.00 9 oral presentations ((7 minutes + 3 minutes discussion)) on Pheochromocytoma and paraganglioma (PHEO/PGL) (Ball Room)**

***Chairs: Massimo Mannelli and Graeme Eisenhofer***

**OR23 14.30-14.40**

**SDH mutations establish a hypermethylator phenotype in paraganglioma**

Eric Letouzé, Cosimo Martinelli, Céline Lorient, Nelly Burnichon, Chris Ottolenghi, Mélanie Ménara, Alexandre Buffet, Jérôme Bertherat, Laurence Amar, Pierre Rustin, Aurélien De Reyniés, Anne-Paule Gimenez-Roqueplo, Judith Favier

**OR24 14.40-14.50**

**TERT promoter mutations in tumors originating from the adrenal gland and extra-adrenal paraganglia**

Thomas G. Papathomas, Lindsey Oudijk, Ellen C. Zwarthoff, Edward Post, Floor A. Duijkers, Max M. van Noesel, Leo J. Hofland, Patrick J. Pollard, Eamonn R. Maher, David F. Restuccia, Richard A. Feelders, Gaston J.H. Franssen, Henri J. Timmers, Stefan Sleijfer, Wouter W. de Herder, Ronald R. de Krijger, Winand N.M. Dinjens, Esther Korpershoek

**OR25 14.50-15.00**

**Heterogenous genetic background of coexistence of pheochromocytoma/paraganglioma and pituitary adenoma**

Judit Dénes, Francesca Swords, Paraskevi Xekouki, Eleanor Rattenberry, Karen Stals, Ajith Kumar, Christopher Wassif, Naomi Fersht, Stephanie Baldeweg, Damian Morris, Stafford Lightman, Amar Agha, Aled Rees, Joan Grieve, Michael Powell, Cesar Luiz Boguszewski, Pinaki Dutta, Rajesh V Thakker, Umasuthan Srirangalingam, Chris J Thompson, Maralyn Druce, Claire Higham, Julian Davis, Mark Stevenson, Brendan O'Sullivan, Phillipe Taniere, Kassiani Skordilis, Plamena Gabrovska, Anne Barlier, Susan M Webb, Anna Aulinas, William M. Drake, John Bevan, Cristina Preda, Nadezhda Dalantaeva, Antônio Ribeiro-Oliveira Jr, Ashley B. Grossman, Jacqueline Trouillas, Sian Ellard, Eamonn Maher, Constantine A. Stratakis, Federico Roncaroli, Márta Korbonits

**OR26 15.00-15.10**

**Opposing effects of HIF1 $\alpha$  and HIF2 $\alpha$  on chromaffin cell phenotypic features and tumor cell proliferation: insights from MAX**

Nan Qin, Aguirre A. de Cubas, Ruben Garcia-Martin, Susan Richter, Mirko Peitzsch, Mario Menschikowski, Jacques W. M. Lenders, Henry Timmers, Massimo Mannelli, Giuseppe Opocher, Matina Economopoulou, Gabriele Siegert, Triantafyllos Chavakis, Karel Pacak, Mercedes Robledo, Graeme Eisenhofer

**OR27 15.10-15.20**

**The bone morphogenic protein 7 (Bmp7) plays a pro-tumorigenic role in pheochromocytoma**

Ines Repokis, Ines Höfig, Natasa Anastasof, Felix Beuschlein, Ronald R de Krijger, Michael John Atkinson, Natalia S. Pellegata

**OR28 15.20-15.30**

**Germline and somatic mosaicism in HIF2A-related polycythaemia-paraganglioma syndrome**

Alexandre Buffet, Sarra Smati, Ludovic Mansuy, Mélanie Ménara, Maëlle Lebras, Marie-Françoise Heymann, Christophe Simian, Judith Favier, Arnaud Murat, Bertrand Cariou, Anne-Paule Gimenez-Roqueplo

**OR29 15.30-15.40**

**Acute catecholamine cardiomyopathy in patients with pheochromocytoma or paraganglioma**

Giavarini A, Chedid A, Bobrie G, Plouin PF, Hagegravege A, Amar L

**OR30 15.40-15.50**

**Correlation between in vivo 18F-fluorodeoxyglucose PET and immunohistochemical markers of glucose uptake and metabolism in pheochromocytoma and paraganglioma**

A. van Berkel, J.U. Rao, B. Kusters, J.W.M Lenders, T. Demir, E. Visser, A.R. Mensenkamp, J.A.W.M. van der Laak, E. Oosterwijk, O.C. Boerman, F.C. Sweep, R.A. Wevers, A.R. Hermus, H.P.M. Kunst, K. Pacak, M. Gotthardt, H.J.L.M. Timmers

**OR31 15.50-16.00**

**Seasonal variation of plasma free normetanephrine concentrations: implications for biochemical diagnosis of pheochromocytoma**

Christina Pamporaki, Michael Bursztyn, Manja Reimann, Tjalf Ziemssen, Stefan R. Bornstein, Fred C.G.J. Sweep, Jacques W.M. Lenders, Graeme Eisenhofer

*16.00-16.30 Conclusions, poster awards and farewell, welcome for the 2014 meeting in Nice*

**List of posters:**

**P1-16 ACC**

**P1 c-myc modulation affects drug responsivity in adrenocortical cancer cells**

L. Cerquetti, C. Sampaoli, R. Marchese, P. Fiore, B. Bucci, P. Lardo, V. Toscano, A. Stigliano

**P2 Primary cell culture of adrenocortical carcinoma (ACC) as a model to predict in-vivo mitotane sensitivity**

Arianna Ardito, Antonina Germano, Barbara Zaggia, Vittoria Basile, Valentina Bellino, Chiara Sciolla, Fulvia Daffara, Massimo Terzolo

**P3 EGFR mutation status in adrenocortical tumors, rational for screening towards personalized medicine.**

Fredrik Wikander, Rajani Maharjan, Tobias Akerström, Joakim Crona, Peter Stölberg, Per Hellman, Peyman Björklund

**P4 Identification of EZH2 as a new actor of malignant progression in adrenal cortex carcinoma**

Drelon Coralie, Berthon Annabel, Ragazzon Bruno, Tissier Frédérique, Kuick Rork, Giordano Tom, Assié Guillaume, Batisse-Lignier Marie, Tauveron Igor, Sahut-Barnola Isabelle, Lefrançois-Martinez Anne-Marie, Bertherat Jérôme, Martinez Antoine, Val Pierre

- P5 Switching off Wnt/ $\beta$ -catenin signaling with new drugs in adrenocortical cell tumors**  
Beatrice Rubin, Raffaele Pezzani, Maria Verena Cicala, Maurizio Iacobone, Carla Scaroni, Franco Mantero
- P6 Binding of Helix Pomatia agglutinin glycoproteins is a predictor of poor survival in adrenal cancers**  
Radu Mihai, Mo Heetun, Gregory P Sadler, Susan Brooks, Parameswaran Rajeev
- P7 Glucocorticoids are involved in the regulation of circadian expressed genes in H295R cell line**  
Zsolt Nagy, Henriett Butz, Istvan Liko, Karoly Racz, Attila Patocs
- P8 Establishment of patient-individual tumor models for endocrine tumors**  
Constanze Hantel, Franzi Scheller, Alexandra Ozimek, Costanza Chiapponi, Thomas Mussack, Felix Beuschlein
- P9 The laterality of adrenocortical carcinoma is different from pheochromocytoma - data from a literature search and the German Adrenocortical Carcinoma Registry**  
Margarita Bala, Cristina L. Ronchi, Matthias Kroiss, Bruno Allolio, Martin Fassnacht on behalf of the German Adrenocortical Carcinoma Study Group
- P10 Incidentally found adrenocortical cancer (ACC) in a group of 2500 patients with adrenal incidentalomas observed at a single endocrinological unit**  
Anna A Kasperlik-Zaluska, Andrzej Cichocki, Maciej Otto, Katarzyna Roszkowska, Rafal Z Slapa, Elzbieta Roslonowska, Jadwiga Slowinska-Szrednicka, Wojciech Jeske, Piotr Dudek, Wojciech Zgliczynski
- P11 CRYOABLATION and dynamic hip screw internal fixation of a painful sclerotic adrenocortical cancer bone metastasis in the proximal femur: a multidisciplinary approach**  
Freitas R., Fragoso MCBV, Grasel CF, Lerario AM, Mendonça BB,, Buendia LA, Naim R, Gangi A
- P12 Laparoscopic surgery for malignant and potentially malignant adrenal tumors**  
GN Zografos, I Perysinakis, I Spyridakis, A Nixon, A Diamantopoulos, E Kyrodinou
- P13 Prognostic parameters in Adrenocortical Carcinoma**  
George Zografos, Eleftherios Chatzellis, George Boutzios, Efi Kyrodinou, Dimitris Thomas, Gregory Kaltsas
- P14 Suspected metastatic Adrenocortical Carcinoma revealing as Pulmonary Kaposi Sarcoma in Adrenal Cushing`s syndrome**  
Margarita Bala, Cristina L. Ronchi, Josef Pichl, Vanessa Wild, Bruno Allolio, Stefanie Hahner

**P15 Cerebral metastases – a very rare presentation of adrenocortical cancer**

Radu Mihai, Derek Roskell, Andrew Weaver

**P16 Efficacy of mitotane in adrenal carcinoma: a case report**

Zampetti B, Grossrubastcher E, Dalino Ciaramella P, Vanzulli A, Loli P

**P17-31 PHEO/PGL**

**P17 Characterization of a novel fluorescence-based animal model of pheochromocytoma**

Ullrich M, Bergmann R, Pietzsch J, Schally AV, Cartellieri M, Chavakis T, Qin N, Peitzsch M, Eisenhofer G, Bornstein SR, Ziegler CG

**P18 Anti-cancer Potential of MAPK Pathway Inhibition in Paragangliomas – Effect of Different Statins on Mouse Pheochromocytoma Cells**

Stephanie M.J. Fliedner, Tobias Engel, Nikoletta K. Lendvai, Angela Oldoerp, Uma Shankavaram, Svenja Nölting, Robert Wesley, Abdel Elkalouhn, Hendrik Ungefroren, Gary Lampert, Hendrik Lehnert, Henri Timmers, Karel Pacak

**P19 A novel somatic SDHA mutation in pheochromocytoma identified by targeted next generation sequencing.**

Joakim Crona, Rajani Maharjan, Margareta Nordling, Peter Stölberg, Per Hellman, Peyman Björklund

**P20 Targeted Next Generation Sequencing reveals frequent somatic NF1 mutations in pheochromocytoma**

Joakim Crona, Rajani Maharjan, Peter Stölberg, Per Hellman, Peyman Björklund

**P21 Targeted next generation sequencing of 11 genes associated with pheochromocytoma. Bioinformatic challenges in the clinical diagnostic setting**

Joakim Crona, Viktor Ljungström, Staffan Welin, Martin K. Walz, Per Hellman, Peyman Björklund

**P22 Life-threatening emergencies in patients with pheochromocytoma**

Anna Riester, Dirk Weismann, Marcus Quinkler, Urs Lichtenauer, Roland Halbritter, Christine Spitzweg, Klaus Hallfeldt, Jochen Schopohl, Felix Beuschlein, Martin Reincke

**P23 Prevalence of SDHA mutations and associated clinical spectrum among patients with pheochromocytomas, extra adrenal paragangliomas and glomus tumors**

A.R. Mensenkamp, J.U. Rao, K. van Gassen, B. Kusters, D.H. Kunst, M.H.F. Bongers, J.W.M. Lenders, H.J.L.M. Timmers

**P24 Genotype-specific differences in uptake of 123I-metaiodobenzylguanidine across hereditary and sporadic pheochromocytomas and paragangliomas**

A. van Berkel, J.W.M. Lenders, A.R. Hermus, I. Piscaer, M. Gotthardt, H.J.L.M. Timmers



- P25 The interpretation of the genetic analysis of pheochromocytoma/paraganglioma may be a challenge for the clinician**  
 Letizia Canu, Elena Rapizzi, Benedetta Zampetti, Rossella Fucci, Gabriella Nesi, Susan Richter, Nan Qin, Valentino Giache, Paolo Prosperi, Gabriele Parenti, Andrea Valeri, Tonino Ercolino, Graeme Eisenhofer, Massimo Mannelli
- P26 An intriguing case of Carney Stratakis: SDHA and what else?**  
 Francesca Schiavi, Elisa Taschin, Paola Sartorato, Stefania Zovato, Ronald De Krijger, Ambrogio Fassina, Giuseppe Opocher
- P27 An unusual presentation of a hereditary pheochromocytoma**  
 Zampetti B., Grossrubastcher E., Dalino Ciaramella P., Boniardi M., Pugliese R., Bonacina E., Penco S., Granata S., Giannattasio C., Loli P
- P28 Incidentally discovered pheochromocytoma and subclinical hypercortisolism: clues for a chromaffin-cortical interaction?**  
 Dalino Ciaramella P, Grossrubastcher E, Zampetti B, Giacomoni A, De Carlis L, Petrella D. Loli P
- P29 Pituitary tumors in SDH mutation carriers**  
 Serena Dematti, Giovanna Branz, Giulia Casagrande, Mauro Recla, Paola Sartorato, Stefania Zovato, Francesca Schiavi, Giuseppe Opocher
- P30 Is immunohistochemistry always reliable in detecting SDH-mutated patients?**  
 Elena Rapizzi, Rossella Fucci, Valentino Giachè, Andrea Valeri, Tonino Ercolino, Gabriella Nesi, Letizia Canu, Massimo Mannelli
- P31 Immunohistochemical Characterization of Stem Cell Markers in Pheochromocytomas and Paragangliomas**  
 L. Oudijk, C. Neuhofer, T.G. Papathomas, E. Korpershoek, H. Stoop, J.W. Oosterhuis, M. Smid, D.F. Restuccia, U. Lichtenauer, M. Robledo, M. Mannelli, AP. Gimenez-Roqueplo, W.N.M. Dinjens, F. Beuschlein, R.R. de Krijger
- P-OR32 Succinate:fumarate ratio for identification and stratification of pheochromocytomas and paragangliomas due to SDHx mutations**  
 Susan Richter, Mirko Peitzsch, Elena Rapizzi, Jacques W. Lenders, Nan Qin, Aguirre A. de Cubas, Francesca Schiavi, Jyotsna U. Rao, Felix Beuschlein, Marcus Quinkler, Henri J. Timmers, Giuseppe Opocher, Massimo Mannelli, Karel Pacak, Mercedes Robledo, Graeme Eisenhofer

## **P32-P44**

### **APA + NAPACA**

**P32 WNT/  $\beta$ -catenin Signalling is Activated in Aldosterone Producing Adenomas and Controls Aldosterone Production**

Annabel Berthon, Coralie Drelon, Bruno Ragazzon, Sheerazed Boulkroun, Frédérique Tissier, Laurence Amar, , Benoît Samson-Couterie, Maria-Christina Zennaro, Pierre-François Plouin, Seham Skah, Michelina Plateroti, Hervé Lefebvre, Isabelle Sahut-Barnola, Marie Batisse-Lignier, Guillaume Assié, Anne-Marie Lefrançois-Martinez, Jérôme Bertherat, Antoine Martinez, Pierre Val

**P33 Mutation screening of Yin Yang 2 in a large cohort of adrenocortical tumours**

Tobias Åkerström, Tobias Gustafsson, Rajani Maharjan, Kenko Cupisti, Holger Sven Willenberg, Per Hellman, Peyman Björklund

**P34 Mutation screening of KCNJ3, KCNK3 and KCNK9 in aldosterone producing adenomas**

Tobias Gustavsson, Tobias Akerström, Holger S Willenberg, Kenko Cupisti, Per Hellman, Peyman Björklund

**P35 The influence of KCNJ5 mutation status on cellular composition and GIRK4 expression**

Ana Moser, Tobias Akerström, Holger S. Willenberg, Kenko Cupisti, Per Hellman, Peyman Björklund

**P36 Detection of KCNJ5 variants in aldosterone-secreting adrenal adenoma**

Gabor Nyiro, Istvan Marczell, Nikolette Szucs, Edit Glaz, Miklos Toth, Karoly Racz, Attila Patocs

**P37 Utility of LC-MS/MS based steroid profiling of adrenal venous samples for characterizing patients with primary aldosteronism**

Matthias Haase, Mirko Peitzsch, Tanja Dekkers, Leo J. Schultzekool, Ad R.R.M. Hermus, Fred C.G.J. Sweep, Oliver Vonend, Lars C. Rump, Gerald Antoch, Dirk Blondin, Stefan R. Bornstein, Jacques W. Lenders, Holger S. Willenberg, Jaap Deinum, Graeme Eisenhofer

**P38 Utility of LC-MS/MS based steroid profiling in adrenal venous samples: discrepancies with immunoassay measured cortisol**

Mirko Peitzsch, Tanja Dekkers, Matthias Haase, Leo J. Schultzekool, Ad R.R.M. Hermus, Dirk Blondin, Fred C.G.J. Sweep, Gerald Antoch, Gabriele Siegert, Jacques Lenders, Jaap Deinum, Holger S. Willenberg<sup>3</sup>, Graeme Eisenhofer<sup>1</sup>

**P39 The role of the Bcll and the A3669G polymorphisms of the glucocorticoid receptor gene in patients with hormonally inactive adrenal adenomas**

Orsolya Acs, Bence T. Acs, Karolina Feldman, Istvan Liko, Judit Majnik, Edit Gláz, Miklos Toth, Karoly Racz, Attila Patocs

- P40 Liquid chromatography-tandem mass spectrometry evaluation of urinary free cortisol and cortisone in Cushing's syndrome (CS), adrenal incidentaloma and suspected CS.**  
Ceccato Filippo, Antonelli Giorgia, Barbot Mattia, Cicala Maria Verena, Pezzani Raffaele, Rubin Beatrice, Gatti Rosalba, Schibotto Viviana, Plebani Mario, Scaroni Carla, Mantero Franco
- P41 Immunohistochemical analysis of adrenal cortical tumors**  
Altieri B, Fadda G, Pontecorvi A, Della Casa S.
- P42 State of art on research of new ultrasound methods for evaluation of non-malignant adrenal masses - initial results**  
Rafal Z Slapa, Anna A Kasperlik-Zaluska, Bartosz Migda, Wiesaw S Jakubowski
- P43 Bilateral Massive Adrenal Haemorrhage from an Incidentaloma, precipitated by E.Coli Urinary tract infection**  
Angshuman Maulik, Adil El-Nujumi, Ben Adler
- P44 Rare case of Cushings disease**  
Faiza Qari
- P45 Rare cause of Addisson disease**  
Faiza Qari

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