

ESTP Newsletter 2015 (3)



Editor Zuhal Dincer (zuhal.dincer@novartis.com)

President's column

Dear ESTP members,

It is with great pleasure that I write following our highly enjoyable and successful 2015 ESTP Conference. The annual meeting was held in the UK's newest vet school at the University of Surrey between the 22nd and 25th September, in conjunction with BSTP and together with the IATP Satellite Meeting on the morning of the first day. Despite a drizzly start, the weather became absolutely glorious and was only outmatched by the sheer enthusiasm and good atmosphere among the Congress participants. We had a range of interesting speakers, high scientific quality at all levels, and new advances in pathology were high on the agenda of the presenters. Comments expressed to me during the meeting and since then, have conveyed a feeling of real collaboration between the BSTP, ESTP, Solution Office and the Scientific and Local Organising Committees. It was heartening to see a number of young pathologists embarking on their careers as well, and they were recognized in our awards (IFSTP Award: Jessica Kemmerling; IATP and (young) poster award: Emilie Cloup and ESTP Publication Award: Preethne Böser). We also unveiled quite a few talented dancers among us, including Adam Hargreaves, BSTP President, Matthias Rinke, ESTP Treasurer, and of course Gopi. It's always good to have additional interests outside pathology! The report of the executive committee which I presented at the AGM focused on three key areas: our core activities, our new activities and also our communication within toxicologic pathology.

1. Core Activities

The work of the INHAND committee comprising 15 system working groups is one of the longest running of our core activities, alongside RITA. A big thanks goes to our ESTP representatives in INHAND, Wolfgang Kaufmann (who will be stepping down from the GESC

committee), Thomas Nolte, Susanne Rittinghausen and Rupert Kellner. At the AGM, I also particularly emphasized the need for continued support for RITA by our companies. In these times of austerity, travel is often restricted and less and less time seems to be available for extra-curricular activities. However, the importance of the RITA database in maintaining correlative data for carcinogenicity studies and subsequent drug approval is paramount and we all need to encourage our companies to support this important historical control database. The Classic Examples Meeting took place again in February this year making use of digital pathology and ensuring that ESTP stays at the forefront of trialing and using this technology. As always, the ESTP looks to collaborate with our sister societies, and particular mention was made of the recent OECD Guidelines on Peer Review discussion document where 13 societies endorsed this publication. Another developing core activity is that of Clinical Pathology and Biomarkers which forms the basis of a committee chaired by Aida Diaz-Bayon. This committee collaborates actively with many societies outside our discipline, including the ACCP, ABCAL and ECVCP and ESVCP and we had two speakers at this year's conference on the topic of biomarkers. An interactive session on biomarkers is already in planning for our 2016 conference in Barcelona.

2. New Activities

As part of our commitment to promote our discipline to new potential toxicologic pathologists, one of our members, Anna-Maria Giusti gave a presentation on the generic role of a toxicologic pathologist at the ECVP/ESVP Summer School, held between 6th and 17th July in Bologna. The Summer School serves as fertile ground for introducing our discipline to a cohort of young pathologists who go through a cyclical training programme in preparation for the Board examinations. 65 trainees attended this year and it certainly seemed to provide a useful adjunct to the course, as many students receive little or no information on toxicologic pathology in their traditional veterinary training programmes. As

part of our educational commitment it was also very exciting to see the strides made by our Pathology 2.0 Committee which has organised three webinars to full capacity this year. A big thanks to Franck Chanut, who stepped down as Chair of this committee at the meeting, for all his hard work. I am also pleased to say that, by the end of the conference, we had a new volunteer for the Chair with Thomas Lemarchand taking over from Franck and building upon the team's success. Thank you Thomas! Please also be aware of another new activity of the ESTP this year. There will be an ESTP survey appearing very shortly in your email box! This survey has been prepared largely by Lars Mecklenburg and Erio Barale and the statistician in charge, John Fry, was also present at our meeting. This forms a key role of establishing up-to-date industry and age-related demographics, job roles and remuneration (all anonymised of course!) which is of interest to the whole membership, and also the ESTP Board, as we consider the needs of our profession and perhaps a new direction in future initiatives. Finally, in another new initiative, a big thanks must go to Gabriele Pohlmeier-Esch, Wolfgang Kaufmann and Xavier Palazzi on their successful Adversity Workshop in June. The workshop brought together experts from the different Tox. Path. Societies and US, European and UK regulatory body representatives to define a working definition of "adverse". There will be a forthcoming publication on this work, alongside a similar publication by the SRPC Committee of the STP.

3. Communication within the discipline of Toxicologic Pathology

A big thanks of course to Zuhail Dincer who provides a quarterly Newsletter for the Society. In addition, as part of our communication and scientific credibility as a society, this year, the topic of the affiliation of our society to a journal was a major point of discussion. The background to re-igniting the discussion is that three years ago, a decision was made to end the contract between Elsevier and the Experimental and Toxicologic Pathology journal based on membership feedback. At that time, the membership had also provided feedback on future initiatives which included that the larger proportion of members wished for a journal affiliation in the future, and that the top two considerations would be the STP Toxicologic Pathology journal or the Journal of Toxicologic Pathology (JSTP). Affiliation to a journal would enable us to have a say in the strategic direction of such a publication, advertisement and promotion of our own society and collaboration with our fellow societies. I would therefore encourage you, whether you receive one of these journals or not, through one of your other society memberships, that you participate in the vote later this month, bearing in mind the advantages for the whole society and its membership.

Finally, thank you to all of the ESTP Executive Committee, for the giving of their "spare" time and many

hours of work to the organization. I look forward to meeting some of you again at the STP/ACVP/ACVCP Society Meeting in Minneapolis this month and if not there, then at the ESTP Meeting in Barcelona, 2016!



Thank you for your membership and support.

Jenny McKay
Your Chairman
jenny-mckay@idexx.com

Presentation at the 13th ECVP/ESVP Summer School on behalf of ESTP – July 16th, 2015, Bologna, Italy

The 13th ECVP/ESVP Summer School took place from Monday 6 July to Friday 17 July 2015 at the Department of Veterinary Medical Sciences at the University of Bologna, Italy, home to one of the oldest universities in the world, founded in 1088. Local organization was provided by Prof. Cinzia Benazzi and her team of young enthusiastic researchers and PhD students who volunteered to cover all the aspects of the logistic of this long meeting. The Summer School is an initiative now successfully established since the first edition started in Nantes in 2003, thought to support the pathologists in training, leading to their eligibility for the European College of Veterinary Pathologist (ECVP) certification. This was the first of the fourth cycle of training program, with each cycle composed of four yearly events with a continuous sequence of programmed topics which (try to) cover the very huge preparation for the ECVP Board Examination. In the modules, covering organ systems and the pathology of specific species, a large percentage of time is usually dedicated to practical training and discussions which provide extensive hands on experience in gross and histopathology.

Altogether, this year there were 65 participants from a highly variable background, with regard to the country of origin, working background/scientific environment and level of experience. Participants came from more than 12

different countries, with higher numbers coming from Spain, Germany, Italy and Romania, followed by Poland, Switzerland, Scandinavia, UK and single participants from outside the EU (Korea, Brazil and Mexico).



Like in previous years, most participants work in academia (92%), and a few in private laboratories (4%) and government (3%). Some just started to work in the field; others had a substantial amount of experience both in the diagnostic aspects of veterinary pathology, but also in the research field.

The participants were welcomed by very sunny and warm Italian midsummer days, but were brave enough to defy the hot and humid climate and follow the excellent program spanning from introductory lesson on Gross, Histopathology and Clinical Pathology to dives in liver pathology and pig pathology, with a two days diversion on Forensic Pathology. When I arrived in Bologna with 38°C and Fata Morgana visions above the horizon I found them actually delighted by a full day of Ocular Pathology with Dr. Emma Scurrrell and Dr. Chiara Giudice, reviewing plenty of slides from case reports from any imaginable species.

And they were resolute enough to stay until late afternoon for my presentation: *Guided tour in an exciting world: the "Industry"*, given on behalf of the ESTP on the roles that a pathologist can cover in the industry. I introduced them to a story of proudness and prejudice, which is to say, the travel of a young enthusiastic veterinary pathologist from academia, who had the prejudice that high level research could only be pursued in universities, and discovered an exciting world of excellence, passion and challenges ultimately leading to the proudness for a work which is cornerstone in the process of discovering and developing new drugs and new chemicals for healthier lives.

The final prize for the attendance's diligence and perseverance was an outstanding Meeting Dinner in a small restaurant hidden in the surrounding hills (the kind of place only known to native people), corroborating the

well-known high level of Bologna's cuisine (for the few who do not know, home of the luscious traditional Lasagne al ragù).

Anna Maria Giusti

anna_maria.giusti@roche.com

2015 ESTP Annual Congress September 22-25, Guildford, Surrey, UK

This year's conference entitled "From gene to drugs: an insider's view on cell pathology" was organized as a collaboration between ESTP and BSTP. The meeting took place on the green campus of the University of Surrey in Guildford in the facilities of UK's youngest Veterinary School. The meeting began on Tuesday morning with a very well-received IATP satellite symposium about "Applications of in vivo and ex vivo multimodality imaging in toxicologic pathology". By lunchtime, most participants had managed to reach the venue in spite of a difficult traffic situation in the local area.



Susan Elmore, NIEHS, US, started off the interesting program with an overview on the different types of cell death and received for her work the BSTP Chirukandath Gopinath Award. David Rubinsztein, Cambridge Institute for Medical Research, UK, looked more specifically into neurodegeneration and the therapeutic approaches to enhance autophagy, and was the recipient of the Royal College of Pathologists' sponsored Kohn Lecture Award. The remaining Tuesday afternoon was filled with an update by the INHAND group on the lymphoid system. Interactive sessions were presented by Charlotte Keenan (Keenan ToxPath Consulting, US), Cynthia Willard-Mack (Envigo, US), Susan Elmore (NIEHS, North Carolina), Christine Rühl-Fehlert (Bayer, Germany), Frieke Kuper (TNO, The Netherlands) and Hans Harleman (Fresenius-Kabi, Germany). ViiA Valge-Archer, MedImmune, UK, concluded the first day with a talk on the opportunities of immune therapy in cancer

treatment. In the evening, the welcome reception took place in the atrium of the brand-new building and gave the more than 180 attendees plenty of opportunity for networking.

Wednesday morning was dedicated to gene therapy and cell based therapies. Luigi Naldini, University School of Medicine, Milan, Italy, gave an overview of his impressive work in the gene therapy field. He illustrated the successes and setbacks in gene therapy treatment of Wiskott-Aldrich syndrome and metachromatic leukodystrophy. Luigi Naldini received the Kettle Lecture Award sponsored by the Royal College of Pathologists. The next speaker, Maria Galli (Rome, Italy), gave the regulator's view, applying a case-by-case approach in this special therapeutic area. Patrizia Cristofori (GSK, UK) illustrated the challenges faced when building up a state-of-the-art GLP facility in two years' time to conduct gene therapy studies. Franck Chanut (GSK, UK) nicely summarized histopathology findings in mouse models used in stem cell transplantation studies. Attilio Bondanza, University School of Medicine, Milan, Italy, talked about models in mice to study cancer immunotherapies in genetically targeted T cell and Dominique Brees, Novartis, Switzerland, presented the challenges of safety testing of T cell and CAR-based therapies. Julia Baker (Charles River, US) gave an overview of toxicity testing of stem cell-derived products, becoming increasingly important in our field with currently over 300 ongoing clinical trials. Kyle Kolaja (Cellular Dynamics, US) demonstrated the opportunities offered by cardiomyocyte stem cells to drug discovery. Giulia Leoni, Catapult, UK, stressed the need for a case-by-case risk-based approach for the development of cell therapies. In between these scientific sessions, the exhibitors had the opportunity to summarize their services in 2-minute slots.



Thursday morning was dedicated to animal models. Dominic Wells, London Veterinary College, UK, shared his experience in neuromuscular disease models. Cory Brayton (Johns Hopkins School of Medicine, US) demonstrated the importance of properly understanding and characterizing our mouse models. She gave numerous examples of confounding factors in mouse

research leading to poor science, possibly resulting in financial losses, which gave rise to a lively debate with the audience. Dominique Brees (Novartis, Switzerland) presented drug discovery projects in which clinical safety questions could be addressed successfully with the help of preclinical models. Caroline Zeiss (Yale University School of Medicine, US) focused on the translational aspects of neurologic models. During the clinical pathology session, Calvert Loudon (Johnson & Johnson, US) discussed the challenging search for the holy grail in the field of drug-induced vascular injury biomarkers, followed by Jarig Darbès (MSD, France), with an update on renal biomarkers. Philippe Couttet (Novartis, Switzerland) commented on the progress of the HESI's Genomics Committee. The Thursday's scientific program was completed by interactive cases, presented by Paul Howroyd (on behalf of Pierluigi Fant, WIL research, France), and Pierre Maliver (Roche, Switzerland).

The conference dinner took place in the stunning location of nearby Loseley Park. After a drink in the Great Hall of Loseley House, we couldn't but admire the beautiful garden and enjoy dinner in this magnificent location.



ESTP conference photos taken by Wolfgang Kaufmann (Many thanks Wolfgang!)



After speeches and awards were given, the dancefloor was opened by the presidents of the organizing Societies, ESTP chairwoman Jenny McKay and BSTP chairman Adam Hargreaves, with several colleagues dancing until late after midnight.

Friday morning's topic was tools and techniques: Jennifer Cann (MedImmune, US) presented the fundamentals of histopathologic image analysis, Jürgen Funk (Roche, Switzerland) discussed novelties in ISH and ISH/IHC double stains and Kuno Würsch (Novartis, Switzerland) gave an interactive presentation on data visualization and communication. The conference finished with some more engaging interactive cases brought by Esther Sutter (Novartis, Switzerland), Peter Maslej (CiToxLAB, Hungary) and Stephanie Klein (AstraZeneca, UK).

And of course our exhibitors and their short presentations of their products! Many thanks to all and hope to see them next year again.

Final appreciation goes to our local organizers, Aude Roulois, Vanessa Schumacher and Franck Chanut and the scientific organizing committee! They did a tremendous job and managed to put together an outstanding program, making the 2015 ESTP congress into another very successful ESTP meeting.

Annabelle Heier
annabelle.heier@novartis.com

ESTP AWARDS

- The Chirukandath Gopinath Lecture Award sponsored by the British Society of Toxicological Pathology (BSTP) 
- The Edgar Hartley Kettle Lecture Award sponsored by the Royal College of Pathologists 
- The Joachim Kohn Lecture Award sponsored by the Royal College of Pathologists 
- The ESTP Publication Award sponsored by Novartis 
- The Award for the Best Poster sponsored by the French Society of Toxicologic Pathology (SFPT) 
- The Charles Capen Trainee Award sponsored by the International Academy of Toxicologic Pathology (IATP) 
- The IFSTP Trainee Award sponsored by the International Federation of Societies of Toxicologic Pathology (IFSTP) 

The society offers two awards alternating every year:

1. Award for Scientific Publication (sponsored by Novartis)

The award for scientific publication (award certificate, prize money, and one year free ESTP membership) is given to an outstanding publication on all aspects of toxicologic pathology of the two preceding years. The applicant should be the main author. Everyone can apply.

2. Award for a thesis (currently funded by the ESTP)

This award consists of first, second and third prize with award certificate, prize money and one year free ESTP membership). With this endowment it is attempted to promote co-operation between Universities and industry and to interest young scientists in toxicological pathology and related fields. Doctoral theses or PhD-theses on any aspect of toxicologic pathology, laboratory animal pathology or experimental pathology will be considered for an award. Applicants have to be enrolled in a European University. Theses have to be written in English or the applicant must be willing to arrange for translation if requested. Theses of the two previous years are considered. The ESTP is currently looking for a (co)sponsor for this award.

The announcements are made in summer every year, evaluation and discussion by the awards committee is done until end of August. Presentation of the awards takes place at the yearly ESTP conference. Next year (2016) it will be the turn of the thesis award. Any member of ESTP who is interested in participating in the awards committee is welcome to contact:

Heike Antje Marxfeld, PhD, DiplECVP BASF SE
 Postal Address:
 BASF SE, GV/TD - Z470, 67056 Ludwigshafen
 Germany
 Phone: +49 621 60-56299 Fax: +49 621 60-51734
 E-Mail: heike-antje.marxfeld@basf.com

ESTP awards committee members are:
 Dr. Elodie Drevon-Gaillot, Dr. Regis Masson, Dr. Lars Mecklenburg, Dr. Thomas Nolte, Dr. Alok Sharma, Dr.

Andrew Spencer, Dr. Annika Herrmann, Dr. Heike Marxfeld

The French Society of Toxicologic Pathology presents two poster awards (prize money 1000€) at each ESTP conference, one for younger researchers and one general award.

The Gopinath award (engraved glass award) is presented by the British Society of Toxicologic Pathology. It is given to the speaker of the lecture funded by the BSTP every year at the ESTP conference. The speaker is an internationally recognized scientist and is chosen by the scientific organizing committee and approved by the BSTP council.

Heike Marxfeld
(On behalf of ESTP award committee)
heike-antje.marxfeld@basf.com

ESTP International Expert Workshop on the general definition and use of "adversity" – UPDATE –

Dear ESTP members,

Our ESTP International Expert Workshop on the general definition and use of "adversity" has now reached its final phase. It comprised of 21 international expert pathologists and toxicologists from the pharmaceutical and chemical industry, contract research organizations and international regulatory authorities (Europe, USA, Japan). After a total of five preparatory teleconferences, a face-to-face meeting was held in Alfortville (Paris), France on 8-9 June, 2015. This was perfectly hosted by Sanofi. An additional audience of over 40 European pathologists and toxicologists enriched the discussions. Workshop members presented the various aspects of adversity during TC's or in Alfortville.

As major achievements of the workshop, a working definition and a tiered approach to adversity were recommended. This approach stipulates "determinants" (decisive factors) which provide rationale and context for identifying a test item-related effect as adverse, as well as further "characteristics" which add explanation and help to achieve precision, but should not be used as primary determinants. Among the characteristics, the most interesting discussion point was adversity related to Mode of Action. It was agreed that pharmacology cannot automatically preclude a finding from being adverse. However, the working group recognized that some threshold should be taken into account between intended pharmacology and exaggerated pharmacology. Some pharmacologic findings might be adverse at certain doses, especially if unintended or severe, while minor

MoA-related changes might be considered non-adverse in a given context. The discussion of this point is still ongoing, showing how complex this aspect is!

Results of the workshop were presented in a poster at the ESTP meeting and will also be presented at the upcoming STP/ACVP meeting in Minneapolis. Most workshop contributions will be made available to a broad audience by two webinars in October (information already sent out by e-mail). Furthermore, the group has drafted workshop results and plans to submit them as publication in *Toxicologic Pathology*, before the end of this year.

We are currently looking into the possibility of conducting a new ESTP International Expert Workshop in 2016 (topic: "adversity of lysosomal storage") and hope to be able to attach its face-to-face part to the congress in Barcelona. Please feel invited to contact us any time in case you have suggestions or wish to receive further information.

Wolfgang Kaufmann
wolfgang.kaufmann@merckgroup.com

Xavier Palazzi
xavier.palazzi@sanofi.com

Gabriele Pohlmeier-Esch
gpe@kaleidis-consultancy.com

Classic Examples in Toxicologic Pathology XXIII – ANNOUNCEMENT –

For many of us, the "Classic Examples" in Hannover are an important date in the calendar: it is the first important scientific meeting and the first occasion in the year to meet colleagues and friends. Our next year's seminar will take place on, February 19 and 20, 2016. As in the past, it will be jointly organized by the Hannover Graduate School for Veterinary Pathobiology, Neuroinfectiology, and Translational Medicine (HGNI) and the Department of Pathology of the University of Veterinary Medicine in Hannover and the ESTP. It will take place at the Department of Pathology of the University of Veterinary Medicine in Hannover, Bünteweg 17.

At this year's seminar, for the first time electronic slides were provided from those lesions, for which preparation of the required 60 slides was not possible. The experience of the participants with the new technique was assessed after the seminar by a survey. Most participants preferred the demonstration of the histopathologic lesions by projector presentation of the scanned slides over the live video demonstration of glass

slides with a microscope. However, the possibility to examine the lesions with a microscope during the seminar was also important for the clear majority of participants. We have considered this feedback for our next seminar: Sixty sets of glass slides will be provided for in maximum 120 participants. In addition, all slides to be shown, and also those from which the full set of recuts cannot be prepared, will be digitalized and demonstrated with a projector during the seminar. Registrants will have on-line access to the digital slides some weeks prior and after the seminar.

Examples of toxicologic pathology will be presented and discussed by the participants. As a novelty, we will include an interactive presentation of therapeutic concepts in oncology. Based on the participants' feedback we will decide whether or not to continue with such kind of presentations in future seminars, e.g. on specific aspects in drug development or new technologies. Our preliminary program for next year includes presentations on the following topics:

- Complex 1 inhibitors
- Glucagon agonists
- Antibody-induced kidney lesions
- Depot-formulations – link between histopathology and toxicokinetics
- Rodent liver foci
- Chemically induced sperm granulomas
- Therapeutic concepts in oncology – past, presence and future
- Aurora-B inhibitors
- Amorphous silicate

All ESTP members will be informed by e-mail when the seminar is open for registration.

Thomas Nolte

[on behalf of Organising Committee (Prof. Dr. Wolfgang Baumgaertner, Prof. Dr. Ulrich Deschl, Dr. Florian Colbatzky, Dr. Thomas Nolte)]

thomas.nolte@boehringer-ingenelheim.com

RITA – Registry of Industrial Toxicology Animal-data – ANNOUNCEMENT –

RITA is an industry sponsored project for generation and maintenance of a historical database for control animals from rodent carcinogenicity studies including conventional studies in rats, mice, and hamsters as well as short-term carcinogenicity studies in transgenic rasH2 mice. Furthermore, tumors in young animals recently gained interest and the group is seeking to expand its focus to individual animals from short-term studies.

Panel meetings in 2016

Panel meetings will start on Monday at 1:00 PM and will last until Wednesday noon. An exception will be the first panel meeting next year, which will be held from Wednesday to Friday, February 17 – 19. This will give participants the opportunity to attend the seminar “Classic Examples”, which will begin subsequently, on Friday, February 19, 1:00 PM. In the past, this scheduling has proven attractive in particular for colleagues coming from overseas.

After we prolonged panel meetings from the former 1 ½ days to two days it was possible to reduce the annual number of meetings from five to four. As an exception, we can plan for only three meetings next year due to budget limitations in the last year of the current contract period. The schedule of meetings in 2016 is:

- February 17 – 19
- June 06 - 08
- October 17 – 19

The ‘microscope panel’ meetings of the RITA group are open to guests from regulatory agencies, non-RITA companies, contract laboratories and universities. The number of guests is limited to three, for organizational reasons. Guests will be charged 50 € covering lunches and beverages and must contact the organizer four weeks in advance of a meeting (Dr. Rupert Kellner, Tel.: +49 511 5350 106; e-mail: rita.panel@item.fraunhofer.de).

The current status of the database

The RITA project is running now for 26 years. Companies participating are: AbbVie, Amgen, AstraZeneca, BASF SE, Bayer AG, Boehringer Ingelheim Pharma GmbH & Co. KG, F. Hoffmann-La Roche Ltd., Merck-Serono, Novartis Pharma AG, Novo Nordisk A/S, Sanofi-Aventis, Syngenta and Takeda Pharmaceutical Company Ltd.

Currently, the database contains 182 rat studies with almost 29,000 primary tumors and more than 32,800 preneoplastic lesions. The 85 conventional mouse studies in the database include about 7,500 primary tumors and 4,500 preneoplastic lesions. In addition, there are 7 transgenic mouse studies and 8 with positive controls. The first three hamster studies include more than 500 primary tumors and more than 1,000 preneoplastic lesions.

For more information see below link:

<http://reni.item.fraunhofer.de/reni/public/rita/index.php>

Thomas Nolte (Chair)

thomas.nolte@boehringer-ingenelheim.com

Matthias Rinke (Co-Chair)

matthias.rinke@bayer.com