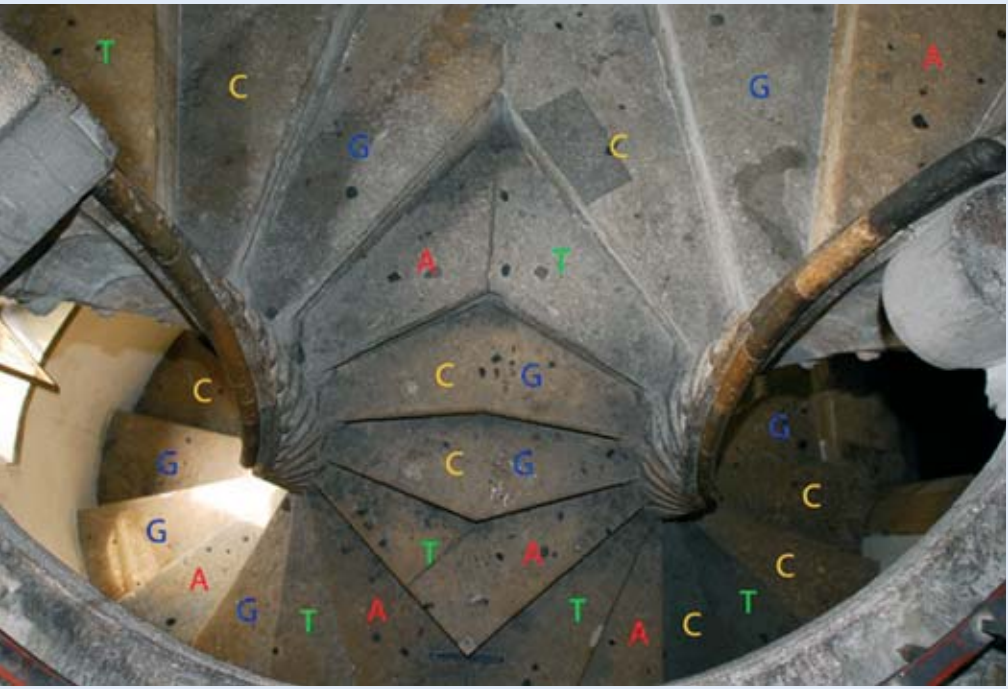
Program

Pannonia Congress of Pathology



Spring Congress of the Austrian, Croatian, Hungarian and Slovenian Societies of Pathology and IAP Divisions

Graz, Austria, March 3–6, 2010

ID1775;01/2010

Die personalisierte 1st line Therapie beim fortgeschrittenen NSCLC mit EGFR M+

- Zugelassen als erste orale 1st line Monotherapie des NSCLC mit aktivierenden Mutationen der EGFR-TK[1] (EGFR M+)
- Signifikante Verlängerung des progressionsfreien Überlebens um 3,2 Monate bei fortgeschrittenem NSCLC im Vergleich zur Chemotherapie[1,2]

Referenzen:
1. Mok TS, Wu Y-L, Thongprasert S, et al. Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. N Eng J Med 2009; 361
2. Carboplatin/Paclitaxel

Fachkurzinformation siehe Seite 17

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Dear Colleagues!

On behalf of the Presidents of the Austrian, Croatian, Hungarian, and Slovenian Societies of Pathology and the respective Divisions of the IAP we would like to invite you to attend the Pannonia Congress in Graz Austria, March 4–6, 2010.

The program of the congress is focused on Lung, Head & Neck, and Bone & Soft Tissue tumors. Additional sessions will cover preneoplasia, common inflammatory processes, and others.

Slide courses have been prepared for these organ topics. A precongress internet access is provided via the Austrian Society homepage (see below).

We have organized lunch satellite symposia on targeted therapy and the impact of pathology in this field.

Molecular pathology as a relevant method is included in the presentations.

March 3, two pre-congress laboratory courses have been organized for EGF receptor mutation test methodology and on FISH/CISH/SISH result interpretation. The lab courses aim on technicians (EGFR mutation test) and young academic colleagues (amplification, translocation in tumor diagnosis).

A social dinner is included in the registration fee and will be held in the Old University of Graz. Since space is limited, seats are given to those, registered early on.

The city of Graz is located in the southeastern part of Austria and can easily be reached by plane – several daily flight connections with Frankfurt, Munich, and Vienna airports and by car, because the highways A2 (Vienna to Villach) and A9 (Slovenian border to Wels) cross in Graz.

The Presidents and Secretaries of the four Societies would be delighted to welcome you here in Graz.

Helmut H. Popper
Ulrike Gruber-Moesenbacher
Austrian Society Pathology/IAP

József Timár / Zsuzsa Schaff
Attila Zalatnai
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Damir Babic
Sven Seiwerth
Croatian Society Pathology

Izidor Kern
Metka Volavsek
Slovenian Society Pathology
& Forensic Medicine

General Information

Organizing Committee:

Prof. Dr. Helmut Popper and OA Dr. Ulrike Gruber-Mösenbacher
Prof. Dr. József Timár, Prof. Dr. Janina Kulka and Dr. Attila Zalatnai
Dr. Izidor Kern and Doc. Dr. Metka Volavsek
Prof. Dr. Damir Babic and Prof. Dr. Sven Seiwerth

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Michael Vesely, Austria
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Attila Zalatnai, Hungary
Nina Zidar, Slovenia

Course Faculty for Technicians

Iris Halbwedl
Andrea Hofmann
Tina Reisenhofer
Gerlinde Winter

General Information

Registration and Hotel information

Congress Bureau:

Karin Lichtenegger
Institute of Pathology
Medical University of Graz
Auenbruggerplatz 25
A-8036 Graz, Austria
Phone: (+43/316) 380 4418
Fax: (+43/316) 385 3432
E-mail: office@pathology.at

On-site Organization:

Katalin Matray
K&M Congress Ltd.
H-1028 Budapest, Hidegkuti ut 153.
Phone: +36-1-301-2000
Fax: +36-1-301-2001
E-mail: katalin.matray@kmcongress.com

For **Hotel reservation** go to www.pathology.at; enter at: PathologInnen and further on ÖGP/IAP Tagungen; there you will find Frühjahrstagung 2010. Below you will find the hotel registration online.
In addition there are rooms available under specific conditions at the Romantik Park Hotel.

*This exclusive hotel is situated in the historical city center of Graz, the **walking distance to the congress site is about 5 to 8 minutes**. The hotel's excellent restaurant offers sophisticated regional cuisine in an elegant setting. It also provides a SPA which includes sauna, indoor-pool and fitness area. The stylish rooms feature all necessities for a comfortable stay. They include elegant bathrooms, air condition, cable TV, mini-bar, radio, hair dryer and telephones with data port etc. http://www.parkhotel-graz.at/.*

For you as a participant at the Pannonia Congress the Parkhotel will offer you the following exceptional rates (valid until the end of January):

Comfort Single Room	€ 101,– a day
Double Room (double occupation)	€ 160,– a day
Double Room (single used)	€ 117,– a day

The rates include a rich breakfast buffet, free parking on hotel premises, use of the business center and the spa facilities as well as all taxes. Bathrobes are provided in the room.

If you like to take this opportunity please contact the ROMANTIK PARKHOTEL by telephone, fax or mail:

CODE WORD: PANNONIA 2010
Phone: (+43/316) 3630-27
Fax: (+43/316) 3630-50
E-mail: romantik.sales@parkhotel-graz.at

General Information

Poster Sessions:

Abstracts for Poster Presentations should be sent to: office@pathology.at
Acceptance of abstracts will be notified directly via E-mail. Abstracts will be published in a supplimentary issue of Pathology & Oncology Research.
At the end of the meeting a poster price will be presented to the two best posters exhibited during the meeting. Poster price jury: J. Timar, S. Seiwerth, S. Lax, N. Gale, M. Volavsek, A. Reiner-Concin, J. Kulka, D. Babic.

For the participants **DFP certificates or equivalents** will be prepared by the congress bureau.

Electronic badges with bar codes are prepared which contain all necessary informations about payment and registration to the dinner and lunch seminars. Please present these badges at the entrance to the registration people.

Speaker's preview room is located in the second floor; follow the signs from the registration desk.

Exhibition Management:

MAW – Medizinische Ausstellungs- und Werbegesellschaft
Freyung 6, 1010 Vienna, Austria
Phone: (+43/1) 536 63-38
Fax: (+43/1) 535 60 16
E-mail: maw@media.co.at

Dates of the meeting

Precongress Lab Course:	March 3, 2010** Institute of Pathology, Microscopy room (FISH, CISH, SISH) and Laboratory for Molecular Pathology (mutation analysis) University Hospital, Auenbruggerplatz 25, Graz
Pannonia Congress:	March 4–6, 2010 Alte Universität Hofgasse 14 (Freiheitsplatz), Graz

Deadlines:

Early registration fee:	January 31, 2010
Abstract submission:	February 4, 2010
Satellite Symposia:	January 31, 2010 *
Precongress course:	January 31, 2010 **

* For the Satellite Symposia there will be no extra charge, but a preregistration until February 1, 2010 is mandatory, because a lunch will be served to those registered. Satellite Symposia cannot be registered onsite!

** For the precongress courses are limited to 15 persons per half-day, so registration is required early on. Multiple registrations from one Institute will not be possible!


Photographer: Karin Bergmann

Registration	Before January 31, 2010	After January 31, 2010	On site
Members of national societies	€ 120.–	€ 140.–	€ 150.–
Non-members of national societies	€ 140.–	€ 160.–	€ 170.–
Technicians and accompanying persons	€ 80.–	€ 100.–	€ 100.–
One day ticket excluding dinner	€ 50.–	€ 50.–	€ 50.–
One day ticket excluding dinner for technicians and accompanying persons	€ 35.–	€ 35.–	€ 35.–
Satellite Symposia: Registration mandatory before February 1, 2010	Free of charge	Free of charge	Free of charge
Precongress course: Registration until January 31, 2010 for one person per institution; Space limited to 15 persons per session	Free of charge	Free of charge	Free of charge

Location Map

Google map of the Inner City of Graz. White arrows mark the Congress venue Old University and the Romantik Park Hotel.

Main Sponsors of the Congress

AstraZeneca

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Roche

Wednesday, March 3, 2010

Laboratory day

Limited number, 15 for each session

BMA (technicians)

Organized by *Gerllinde Winter*
Iris Halbwedl, Andrea Hofmann,
Tina Reisenhofer and Gerllinde Winter

8:30 – 12:00	**EGFR mutation testing**	(Group 1)
13:00 – 16:30	**EGFR mutation testing**	(Group 2)

MD (residents)

Organized by
Cornelia Hauser-Kronberger and Michael Vesely

8:30 – 12:00	**FISH/SISH**	(Group 1)
13:00 – 16:30	**FISH/SISH**	(Group 2)
19:00	Get together party of the participants in the Institute of Pathology, Foyer	
18:00 – 19:00	Sitzung der Institutsleiter und des Vorstandes der ÖGP-IAP; Institut für Pathologie, Auenbruggerplatz 25, Graz, Bibliothek Thema: Wie soll sich das Fach die Pathologie in der Öffentlichkeit darstellen – Wie können wir dies erreichen? *Moderator: Dr. Ernest Pichlbauer, Vienna*	

Thursday, March 4, 2010

Technics Symposium

chaired by
Cornelia Hauser-Kronberger and Michael Vesely
Presentations 12' followed by 3' of discussion

8:15 – 8:30 **K-RAS mutation testing of colorectal and lung carcinomas – an affordable algorythm**
Zita Hegedüs, 2nd Dept. Pathology, Semmelweis University, Budapest

8:30 – 8:45 **Molecular profiling of non-small cell lung cancer**
Mojca Strazisar and Damjan Glavac, Institute of Pathology, Medical Faculty Ljubljana

8:45 – 9:00 **Protein extraction and protein array from formalin fixed paraffin embedded tissues**
Hannelore Kothmaier, Institute of Pathology, Medical University Graz

9:00 – 9:15 **miRNA detection in fixed tissues**
Lisa Arzt, Institute of Pathology, Medical University Graz

9:15 – 9:30 **Optimal handling of surgical specimen to be suitable for molecular examinations**
Violetta Piurkó, 2nd Dept. Pathology, Semmelweis University, Budapest

9:30 – 9:45 **In situ hybridization methods to detect Her2Neu amplification of breast carcinoma**
Katalin Varga, Pathology Dept. National Oncology Institute, Budapest

9:45 – 10:15 **COFFEE BREAK**

10:15 – 10:30 **Tissue microarray applications in pathology**
Tibor Krenács, Budapest

10:30 – 10:45 **Pitfalls in CISH and SISH**
Cornelia Hauser-Kronberger, Institute of Pathology, Hospital and Private University Salzburg

Thursday, March 4, 2010

10:45 – 11:00 **Pitfalls in FISH**
Michael Vesely, Institute of Pathology, Hospital Hietzing, Vienna

11:00 – 11:15 **EGFR status in non small cell lung cancer**
Mitja Rot, University Clinic of Respiratory and Allergic Diseases Golnik

11:15 – 11:30 **Mutation analysis of EGFR and KRAS in daily practice**
Wolfgang Hulla, Institute of Pathology, Kaiser Franz Josef Hospital, Vienna

11:30 – 11:45 **Genetic analysis in Microbiology**
Harald Kirschner, Institute of Pathology, Kaiser Franz Josef Hospital, Vienna

11:45 – 12:00 **SHORT BREAK**

8:30 – 11:45 **Basics in Pathology** — Entrance level, Press Room

Breast Pathology update
Angelika Reiner-Concin

8:30 – 10:00 **Meeting of Pulmonary Pathology Working Group** — Office OG2
chaired by
Ulrike Gruber-Mösenbacher

10:00 – 11:30 **Meeting of Mikrobiology Working Group** — Office OG2
chaired by
Milo Halabi

Thursday, March 4, 2010

Lunch Seminar sponsored by Astra Zeneca

chaired by
Helmut Popper and Damir Babic

EGFR mutation and treatment

12:00 – 12:25 **Recommendations for EGFR testing in NSCLC**
Robert Pirker, Dept. Oncology, Medical University Vienna

12:25 – 12:40 **The role of Pathology in diagnosis and treatment of NSCLC**
Keith Kerr, Institute of Pathology, University of Aberdeen, UK

12:40 – 13:00 **Basis for targeted therapy in NSCLC – EGFR and other targets**
Martin Filipits, Cancer Research Institute, Vienna

13:00 – 13:40 **Poster Session 1**
chaired by
Sigurd Lax and Angelika Reiner-Concin

Symposium on Pulmonary Tumor Pathology

chaired by
Helmut Popper and József Timár

13:40 – 14:00 **The importance of adenocarcinoma subtyping**
Helmut Popper, Institute of Pathology, Medical University Graz

14:00 – 14:20 **Squamous cell carcinoma – variants and markers**
János Fillinger and Ibolya Soltész, Korányi National Pulmonology Institute, Budapest

14:20 – 14:40 **Large cell carcinoma variants and the implication for therapy**
Bruno Murer, Institute of Pathology, Ospedale Dell'Angelo, Zelarino/Mestre, Italy

14:40 – 15:10 **Prognostic and predictive markers in lung carcinomas**
Keith Kerr, Institute of Pathology, University of Aberdeen, UK

15:10 – 15:40 **COFFEE BREAK**

Thursday, March 4, 2010

15:40 – 16:10 **Is there a metastatic signature in lung cancer?**
Marco Chilosi, Dept. Pathology, University of Verona, Italy

16:10 – 16:30 **Smears, bronchial biopsies, transthoracic biopsies – are these sufficient for molecular testing?**
József Tímár, 2nd Dept. of Pathology, Semmelweis University Budapest

16:30 – 16:50 **Childhood lung tumors**
Elisabeth Bruder, Institute of Pathology, University of Basle, Switzerland

16:50 – 17:10 **Are there any news from SCLC?**
Izidor Kern, University Clinic of Respiratory and Allergic Diseases Golnik

17:10 – 18:00 **MScope, the use of the educational and clinical modules**
Pierre Le Fevre, Aurora, Montreal, Canada

Slide Seminar Interstitial Lung Diseases

organized and chaired by
Izidor Kern and Helmut Popper

8:15 – 8:30	**Case 1** *János Fillinger, National Korányi Institute of Pulmonology, Budapest*
8:30 – 8:45	**Case 2** *Elvira Stacher, Institute of Pathology, Medical University Graz*
8:45 – 9:00	**Case 3** *Izidor Kern, University Clinic of Respiratory and Allergic Diseases Golnik*
9:00 – 9:15	**Case 4** *Gerhard Dekan, Institute of Pathology, Medical University Vienna*
9:15 – 9:30	**Case 5** *Georg Hutarew, Institute of Pathology, Hospital and Private University Salzburg*
9:30 – 9:45	**Case 6** *Ulrike Gruber-Mösenbacher, Institute of Pathology, Teaching Hospital Feldkirch*
9:45 – 10:15	**COFFEE BREAK** *sponsored by the Major of the City of Graz, Mag. Siegfried Nagl*
10:15 – 10:30	**Case 7** *Ulrike Setinek, Institute of Pathology, Otto Wagner Hospital, Vienna*
10:30 – 10:45	**Case 8** *Ibolya Soltész, National Korányi Institute of Pulmonology, Budapest*
10:45 – 11:00	**Case 9** *Sven Seiwerth, Institute of Pathology, University of Zagreb*

Friday, March 5, 2010

11:00 – 11:40 **Poster Session 3**
chaired by
Jozsef Timár and Metka Volavsek

11:40 – 12:00 **SHORT BREAK**

Lunch Seminar sponsored by Roche
chaired by
Cord Langner and Felix Offner

12:00 – 12:30 **Her2Neu in gastric carcinomas**
Josef Rüschoff, Pathologie Nordhessen, Kassel, BRD

12:30 – 12:45 **Do we need immunohistochemical staining for Her2Neu in breast carcinomas?**
Josef Rüschoff, Pathologie Nordhessen, Kassel, BRD

12:45 – 13:00 General Discussion

Symposium Head & Neck Pathology
chaired by
Nina Gale and Irene Sulzbacher

13:00 – 13:20 **Squamous intraepithelial lesions of the Larynx**
Nina Gale, Institute of Pathology, Medical Faculty Ljubljana

13:20 – 13:40 **HPV in upper respiratory tract tumors**
Mario Poljak, Institute of Microbiology, Medical Faculty Ljubljana

13:40 – 14:00 **Spindle cell carcinomas of the Head&Neck**
Nina Zidar, Institute of Pathology, Medical Faculty Ljubljana

14:00 – 14:20 **Soft tissue tumors in URT**
Alfred Beham, Institute of Pathology, Medical University Graz

Friday, March 5, 2010

14:20 – 14:35 **EGFR and functional markers in selecting head and neck carcinoma patients for Cetuximab and tyrosine kinase inhibitor treatment**
József Tóvári, National Koranyi Institute of TB and Pulmonology, National Institute of Oncology, Budapest

14:35 – 14:50 **The role of aspiration cytology in the diagnosis of head and neck lumps**
Eszter Székely and Járay Balázs, 2nd Dept. of Pathology, Semmelweis University, Budapest

14:50 – 15:10 **Salivary gland tumors**
Laszlo Vass, Dept. Pathology, Flór Ferenc Hospital, Budapest

15:10 – 15:30 **Odontogenic cysts and tumors**
Spomenka Manojlovic, Institute of Pathology, University of Zagreb

15:30 – 16:00 **COFFEE BREAK**

Symposium on Soft Tissue & Bone Tumors

chaired by
Sven Seiwerth and Alfred Beham

16:00 – 16:30 **Genetics of soft tissue tumors**
Florence Pedeutour, Faculty of Medicine, Laboratory of Solid Tumor Genetics, Nice University Hospital and CNRS UMR

16:30 – 17:00 **The spectrum of myogenic and fibrogenic sarcomas**
Angelo Paolo DeiTos, Anatomic Pathology, General Hospital of Treviso, Treviso

Friday, March 5, 2010

Evening Dinner *sponsert by the Governor of Styria, Mag. Franz Voves, Old University Graz*

19:30 – 20:00 Welcome Cocktail

Welcome by the Governor of Styria, Mag. Franz Voves

Welcome by the Major of the City of Graz, Mag. Siegfried Nagl

Welcome addresses by the Presidents of the four Societies

H. Popper
J. Timar
D. Babic
I. Kern

Between main course and dessert:
Diseases in a Stone Age people at the time of first contact with 20th century medicine
Robin A. Cooke, Editor of IAP News, Australia

Symposium on Soft Tissue & Bone Tumors

continued from March 5
chaired by
Sven Seiwerth and Alfred Beham

8:30 – 8:50 **Sarcoma – what we need to know about diagnosis and signaling pathways?**
Sven Seiwerth, Institute of Pathology, University of Zagreb Synovial

8:50 – 9:10 **Targeted therapy in osteosarcoma – fact or fiction?**
Anne-Marie Cleton-Jansen, Institute of Pathology, Leiden University Medical Center, NL

9:10 – 9:25 **Contemporary GIST pathology**
Bernadette Liegl-Atzwanger, Institute of Pathology, Medical University Graz

9:25 – 9:40 **Vascular tumors of soft tissue**
Janez Lamovec, Institute of Oncology Ljubljana

9:40 – 9:55 **Pediatric soft tissue tumors**
Bozo Kruslin, Institute of Pathology, University of Zagreb

9:55 – 10:10 **FISHING OR SISHING in soft tissue tumors?**
Gábor Méhes, Institute of Pathology, Debrecen

10:10 – 10:30 **COFFEE BREAK**

Slide Seminar Head & Neck Pathology

organized and chaired by
Metka Volavsek and Lászlo Vass

10:30 – 10:45 **Case 1**
Lászlo Vass, Dept. Pathology, Flór Ferenc Hospital, Budapest

10:45 – 11:00 **Case 2**
Balázs Járay, 2nd Dept. of Pathology, Semmelweis University Budapest

11:00 – 11:15 **Case 3**
Nina Gale, Institute of Pathology, Medical Faculty Ljubljana

11.15 – 11:30 **Case 4**
Nina Zidar, Institute of Pathology, Medical Faculty Ljubljana

11:30 – 11:45 **Case 5**
Spomenka Manojlovic, Institute of Pathology, University of Zagreb

11:45 – 12:00 **Case 6**
Metka Volavsek, Institute of Pathology, Medical Faculty Ljubljana

12:00 – 12.15 **Case 7**
Alfred Beham, Institute of Pathology, Medical University Graz

12.15 – 12:30 **Case 8**
Irene Sulzbacher, Medical University of Vienna

Lunch Seminar sponsored by DAKO

chaired by
Spomenka Manojlovic and Attila Zalatnai

12:30 – 13.10 **Diagnostics in the future, a companies perspective**
Mark Bloomfield, Country Manager, DAKO

13.10 – 13:30 **Quality Management in Her2Neu testing**
Representative from DAKO

Saturday, March 6, 2010

Slide Seminar Soft Tissue & Bone Tumors

organized and chaired by
Matej Bracko and Zoltán Sáp

13:30 – 13:45 **Case 1**
Zsolt Orosz, National Institute of Oncology, Budapest

13:45 – 14:00 **Case 2**
Alfred Beham, Medical University Graz

14:00 – 14.15 **Case 3**
Sven Seiwerth, Institute of Pathology, University of Zagreb

14.15 – 14:30 **Case 4**
Susanna Lang, Medical University of Vienna

14:30 – 14:45 **Case 5**
Zoltán Sápi, 1st Dept. of Pathology,
Semmelweis University, Budapest

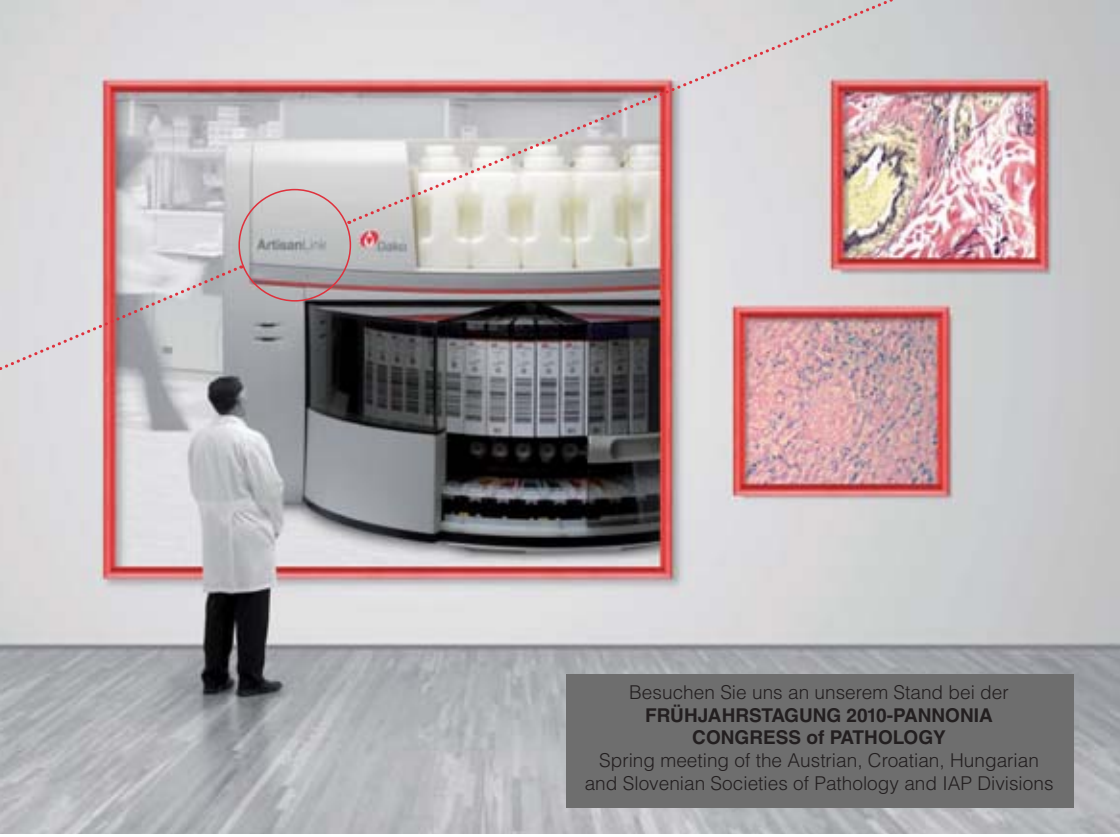
14:45 – 15:00 **Case 6**
Matej Bracko, Department of Pathology,
Institute of Oncology, Ljubljana

15:00 – 15.15 **Case 7**
Snjezana Frkovic Grazio, Department of Pathology,
Institute of Oncology, Ljubljana

15.15 – 15:30 **Case 8**
Tamás Tornóczky, Dept. Pathology, University of Pécs

15:30 – 15:50 **Announcements of the poster awards**

15:50 – 16.10 **Closing remarks by the Presidents**



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Abstract No 1/1

MALT lymphoma arising from Hashimoto's thyreoiditis: a benign lymphoproliferative disorder?

Names and affiliations Mail address of presenter: Tamás Csonka, Ferenc Fazakas, Balázs Dezs, Gábor Méhes Department of Pathology, University of Debrecen, Nagyerdei krt. 98., H-4032 Debrecen, Hungary

Introduction:
The B-cell marginal zone lymphomas of the thyroid gland are rare and develop from reactive lymphoid hyperplasia associated to Hashimoto's thyroiditis. We report on a 80-year-old female patient who had a bilateral subtotal thyroidectomy in July 2000 which was diagnosed as Hashimoto's thyreoiditis after histology. Nine years later she complained a goiter of the residual thyroid gland. The CT scan of the neck region showed a large right thyroid lobe compressing the trachea.

Methods and results:
The removed tissue presented histologically large areas of hyperplastic lymphoid tissue with frequent secondary follicles and an expanded marginal zone. The number of thyroid follicules was decreased and many of them were filled with small compact monocytoid cell balls. While the diffuse lymphatic infiltrate was a mixture of B- and T-cell populations and plasmocytes according to the IHC profile, the intrafollicular monocytoid cells showed homogenous intense postivity for CD20 and CD79a and negativity for CD5, cyclin D1 and Bcl-2. The Mib-1 cell proliferation marker corroborated the impression of an indolent neoplasm with staining of only 2% of the intrafollicular B cells, while up to 20% cell proliferation was observed in the hyperplastic lymphoid infiltrate of the thyroid. To prove the monoclonal neoplastic nature of the lymphoprolifertive change we examined the immunoglubulin heavy chain (IgH) fraction (FR) 2 and 3 with polimerase chain reaction (PCR), which showed a polyclonal arrangement when whole tissue sections were applied. However, laser capture microdissection (LCM) of the intrafollicular B cell balls showed a monoclonal IgH arrangement for both FR2 and FR3. The diagnosis of an indolent marginal zone lymphoma arising from Hashimotho's thyroiditis was stated. Following the review of the surgical specimen removed in the year 2000 we were able to find isolated foci of monocytoid B-cells in an infiltrative intrafollicular fashion identical to the change 9 years later.

Conclusion:
Lymphoid hyperplasia in Hashimoto's thyreoiditis may cover benign clonal lymphoproliferative changes of MALT origin which persist for extreme long time periods without transformation Extranodal MALT lymphoma of the thyroid seems to evolve from this cell population without systemic dissemination in a very slow fashion.

Abstract No 1/2

A case of colon cancer with multiple K-Ras mutations and corresponding clonal segregation to different lymph node metastases

Names and affiliations Mail address of presenter:
Jahn SW[1], Stacher E[1], Stockinger R[2], Spreitzer S[2], Offner F[2], Höfler G[1]
[1] Department for Pathology, Medical University of Graz
[2] Department for Pathology, LKH Feldkirch
Stephan Jahn: stephan.jahn@medunigraz.at

Introduction:
K-Ras mutation status analysis in colorectal cancer has gained paramount importance in predicting response to humanized antibody treatment targeting the EGFR-receptor. Few publications have addressed the question of intratumoral heterogeneity and corresponding patterns of metastatic spread. High concordance rates between primary tumour and metastases are the almost universal finding in the literature.

Methods:
We investigated a case of colon cancer from a 60year old male with a moderately differentiated tubular adenocarcinoma of the coecum pT4pN2 (4/20 lymph nodes). A predominant mucinous tumour differentiation of the primary tumour was observed with one adjacent area demonstrating a non-mucinous tubular differentiation. A corresponding non-mucinous tumor differentiation was noted in one lymph node metastasis while three lymph node metastases showed signs of a mucinous differentiation. Material from primary tumour as well lymph node metastases was selected by laser capture microdissection. Tumour DNA was analyzed for K-Ras mutations by allele specific PCR (ARMS) using the TheraScreen: K-RAS Mutation Kit™ (DxS®) on 31300 Avant Genetic Analyzer™s (Applied Biosystems®) and/or Pyrosequencing (PyroMark KRAS Kit™, Qiagen® on a PyroMark Q24™ sequencer, Quiagen®).

Results:
Intratumoral heterogeneity of K-ras mutation was observed with adjacent areas demonstrating monoclonal mutations at codon 12 of the K-ras gene consisting of GGT->GAT and GGT->GTT mutations respectively. One lymph node metastasis demonstrated clonal GGT->GTT mutation as opposed to three lymph node metastases with clonal GGT-GAT mutation. Furthermore GGT->GAT mutated tumour areas were associated with mucinous differentiation in both primary tumour and metastases as opposed to GGT->GTT mutated tumour areas with a non-mucinous phenotype.

Discussion and Conclusion:
Colorectal adenocarcinoma can demonstrate intratumoral heterogeneity with regard to K-Ras mutational status. Heterogeneity not only applies to mutation versus wild-type heterogeneity but also to the specific type of K-Ras mutation present. Multiple different K-Ras mutations can clonally segregate to different lymph node metastases, which points to K-Ras mutations taking place prior to metastatic spread. Multiple different K-Ras mutations in (lymph)node metastases are not necessarily a sign of multiple primary malignancies. Although therapeutic management is currently not stratified according to the type of K-Ras mutation detected, future therapies might be targeted to specific K-Ras mutations. Detection of K-Ras mutation heterogeneity might, therefore, gain therapeutic importance.

Abstract No 1/3

Tumour Size – an Underestimated Prognostic Variable in Colorectal Cancer?

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Introduction:
T classification, reflecting vertical tumour penetration across the different layers of the bowel wall, remains the strongest prognostic parameter in colorectal cancer (CRC). Our study aimed to investigate the clinical significance of tumour size, in particular the maximum horizontal tumour diameter, in a large cohort of CRC patients.

Methods:
400 patients were randomly sampled from the files of the CRC database of the Institute of Pathology, Medical University of Graz, Austria. Of these, 381 tumours were available for review pathology. Tumour size and location were extracted from the medical history and were known for 359 patients (94%). 107 tumours (28%) were located in the right colon, 110 (29%) in the left colon, and 164 (43%) in the rectum. Receiver-operator characteristic (ROC) analysis was applied to identify the optimal (maximum of sum of sensitivity and specificity) cut-off values with respect to prognostic impact.

Results:
Median tumour size was 4.5 cm (range 0.6-15). Tumour size exceeding 4.5 cm was observed in 159 patients (44%) and was associated with high T and N classification, high UICC stage and poor tumour differentiation. At median follow-up of 59 months, 141 patients (40%) showed tumour progression. While 4.5 cm was identified as the optimal prognostic cut-off value within the whole group of patients, ROC analysis restricted to different parts of the large bowel determined 5 cm, 5.3 cm, 3.9 cm, and 3.4 cm as cut-off values with the strongest discriminatory capacity in colon, right-sided colon, left-sided colon, and rectum cancers, respectively. Within the colon, tumour size exceeding 5 cm proved to be a significant prognostic variable in both univariate and multivariate analyses with respect to prediction of progression-free (RR 2.09, 95% CI 1.25-3.48, p=0.005) and cancer-specific survival (RR 1.86, 95% CI 1.08-3.21, p=0.025). In subgroup analyses applying the above mentioned optimal cut-off values, prognostic impact was particularly strong in right-sided cancers compared with left-sided cancers. Regarding rectal cancers, no independent influence on outcome was noted.

Abstract No 1/3

Discussion and Conclusion:
Tumour size, in particular the maximum horizontal tumour diameter, proved to be an important prognostic parameter for patients with CRC. Optimal cut-off values vary among different parts of the large bowel, decreasing from the right colon to the left, and ultimately to the rectum. While prognostic impact is strong within the colon, it appears to be of minor value within the rectum. Since tumour size is significantly associated with progression-free and cancer-specific survival it may be of importance with respect to surveillance and selection of patients for adjuvant therapy.

Abstract No 1/4

Colorectal Cancer: "Epithelial-Epithelial-Transition (EET)" at the Invasive Front

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Introduction:
Non-neoplastic colorectal mucosa as well as colorectal adenoma and/or carcinoma generally lack expression of keratin 7 (K7). Recent evidence, however, indicates that some colorectal tumours acquire K7 expression during the neoplastic process. This study aimed to assess the prevalence of K7 expression in colorectal cancer (CRC), to correlate findings with clinicopathological parameters and outcome of affected patients, and to evaluate the distribution of K7 expressing cells within tumour tissues.

Methods:
400 patients were randomly sampled from the files of the CRC database of the Institute of Pathology, Medical University of Graz, Austria. Of these, 370 patients were evaluated for K7 expression by immunohistochemistry using a tissue microarray technique and in an additional step by whole section staining. Follow-up data were available for 340 (92%) patients. K7 expression was semiquantitatively scored as either focal (<10%), moderate (10-50%), or extensive (>50%). K7 expression was related to various clinicopathological parameters as well as progression-free and cancer-specific survival.

Results:
32 (9%) tumours were immunoreactive for K7, with 5 cases showing extensive, 4 moderate and 23 focal expression, respectively. K7 expression prevailed in single cells and small cell clusters at the invasion front and was associated with the amount of tumour budding, 20/158 (13%) tumours with high degree of tumour budding (+10 budding foci at x20 objective lens) showed K7 expression compared with 12/212 (6%) tumours with low degree of tumour budding (p=0.02). In addition, K7 expression was significantly associated with poor tumour differentiation, since 18 out of 119 (16%) high grade (G3/G4), yet only 14 out of 251 (6%) low grade (G1/G2) cancers showed K7 immunoreactivity (p=0.005).

Abstract No 1/4

Disease progression occurred in 15/29 (52%) patients with K7-positive tumours and 126/311 (41%) patients with K7-negative tumours (p=0.19, log-rank test). Actuarial 5-year progression-free survival rates for patients with K7-positive and patients with K7-negative tumours were 43% and 60%, respectively. Moreover, 14/29 (48%) patients with K7-positive tumours, yet only 103/311 (33%) patients with K7-negative tumours died of disease (p=0.06, log-rank test). Actuarial 5-year cancer-specific survival rates for patients with K7-positive and patients with K7-negative tumours were 51% and 66%, respectively.

Discussion and Conclusion:
K7 expression is rarely observed in colorectal cancer and is, if present, usually found only in a minority of tumour cells. Remarkably, however, K7-positive tumour cells were found to cluster at the invasive front, correlating with the amount of tumour budding. These changes in the keratin composition of the cytoskeleton illustrate hitherto unrecognized morphological changes occurring during the process of invasion and may, in accordance to the well established concept of epithelial-mesenchymal transition (EMT), tentatively be named "epithelial-epithelial transition (EET)".

Abstract No 1/5

Prognostic Significance of Tumour Necrosis in Colorectal Cancer

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Introduction:
The prognostic impact of tumour necrosis in colorectal cancer (CRC) is still under debate. Our study aimed to evaluate the prognostic significance of tumour necrosis with respect to progression-free and cancer-specific survival in a large cohort of patients and to relate findings to the expression of proteins involved in the control of cancer cell death, such as p53 and bcl-2.

Methods:
381 cancer specimens were retrospectively re-evaluated. Follow-up data were available from 350 (92%) patients, mean and median time of follow-up being 64 and 61 months, respectively. The extent of tumour necrosis was semiquantitatively assessed and recorded as either absent, focal (<10% of the tumour area), moderate (10-30%) or extensive (>30%). Findings were correlated with different clinicopathological parameters as well as the expression of p53 and bcl-2 which was assessed immunohistochemically using a tissue microarray technique and recorded as either positive (using a cut-off value of 10%) or negative.

Results:
Tumour necrosis was noted in 365 (96%) tumours, with 180 (47%) cases showing focal necrosis, 119 (31%) moderate necrosis, and 66 (17%) extensive necrosis, respectively. Extent of necrosis was significantly associated with high T classification ($p<0.001$), high N classification ($p=0.005$), high UICC stage ($p<0.001$), poor tumour differentiation ($p<0.001$), large tumour size ($p<0.001$), and presence of blood vessel invasion ($p=0.01$). Regarding TMA analysis, cancer tissue allowing a reliable evaluation of p53 and bcl-2 immunoreactivity was present in 368 (97%) cases. Distinct nuclear p53 immunoreactivity was observed in 192 (52%) tumours, whereas distinct cytoplasmic bcl-2 immunoreactivity was present in 95 (26%) tumours. We observed no association of tumour necrosis with the expression of p53 and bcl-2.
In Kaplan-Meier analyses using cut-off values of 10% and 30% for assessment of tumour necrosis, prognostic impact was observed regarding both progression-free and cancer-specific survival ($p<0.001$), respectively. Multivariate testing, however, proved only the 30% cut-of value (extensive necrosis) as independent predictor of both disease progression and cancer-specific survival in a model including a collection of well established prognosticators, such as T and N classification and tumour grade. Of note, restricting analysis to UICC stage II patients, only the 10% cut-off value for tumour necrosis proved to be an independent prognostic variable with respect to progression-free, yet not with respect to cancer-specific survival.

Abstract No 1/5

Discussion and Conclusion:
Tumour necrosis is a common finding in CRC, and its extent is significantly associated with T and N classification, UICC stage, tumour size and grade as well as angioinvasion. In addition, tumour necrosis proved to be an independent prognostic parameter with respect to both progression-free and cancer-specific survival. Since tumour necrosis is readily assessable in H&E stained sections, its presence should routinely be commented upon in the pathology report.

Abstract No 1/6

Squamous cell carcinoma of the lung with extensive basement membrane material deposition: report of a case

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Lung cancer is one of the most common cancers in the world and one with the highest mortality rate. Squamous cell carcinomas comprise 44% of lung cancers in men, and 25% in women. Disease stage and performance status at diagnosis are the most powerful prognostic signs but histologic subtype and growth patterns are also important. Basement membrane is important in regulation of cell growth and differentiation. The loss of an intact basal membrane is the initial step in tumor invasion. Carcinomas of different origin with abundant basement membrane depositions were described in the literature. It seems that the patients with extensive basal membrane depositions have favorable prognosis and it might have value as an additional independent prognostic indicator for survival. We describe male patient, 71 years old, with squamous cell carcinoma of the lung, in stage I of the disease. Tumor measured 5 cm in greatest dimension and was in proximity of main bronchus, without lymph node metastases. Microscopically, tumor was composed of cords and nests of poorly differentiated atypical squamous cells, focally with central necrosis. Around tumors nests and in the adjacent tissue massive basal membrane deposits were found. Deposits were more clearly seen with AlcianPAS and Mallory staining.
According to the literature data, well differentiated tumors showed extensive basement membrane deposition and in our case abundant deposits surrounded poorly differentiated atypical squamous cells.

Literature:
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Conn IG et al. Basement membranes in urothelial carcinoma. Br J Urol 1987;60:536-42

Abstract No 1/7

Gastric Cancer and Concomitant Renal Cell Carcinoma – A Systematic Immunohistochemical and Molecular Analysis

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Introduction:
Our study aimed to evaluate 12 patients with concomitant gastric cancer and renal cell carcinoma (RCC) including conventional histology, immunohistochemistry as well as molecular analysis.

Methods:
Clinicopathological and follow-up data were analyzed by chart review and interviewing attending physicians. Basic personal data were compared with that of patients experiencing either gastric cancer or RCC contained in the files of our institute. Histopathology of all tumor probes was reassessed. Immunohistochemistry included p53 expression, proliferative activity (MIB-1), mismatch repair status and E-Cadherin expression for gastric cancers which were additionally analyzed for Epstein-Barr-Encoded-RNA (EBER) by in-situ hybridization (ISH). MSI was analyzed with a PCR multiplex system and capillary electrophoresis. KRAS mutations in codons 12 and 13 were tested by pyrosequencing.

Results:
There were eight males and four females. Time of diagnosis was not significantly early for both cancers. Two patients had additional primary colorectal carcinomas (CRCs). The majority of gastric cancers were poorly differentiated with tumor infiltrating lymphocytes (TILs) being a common finding. All RCCs were of clear cell type, mostly well differentiated and were diagnosed in an early stage. Gastric cancers were rapidly proliferating (MIB-1) ands showed loss of E-cadherin staining in a significant number of cases. Two gastric cancers had a loss of mismatch repair proteins hMLH1 and PMS2, which was confirmed by molecular analysis showing a high degree of microsatellite instability. All RCCs were microsatellite stable. EBV was detected by ISH in one gastric cancer. Pyrosequencing for detection of KRAS mutations was positive in one gastric cancer. Two patients had also KRAS mutations in additional CRCs, while none of the RCCs had KRAS mutations.

Discussion and Conclusion:
Gastric carcinomas had striking histological features in terms of poor differentiation and presence of TILs. In contrast to other studies, this particular phenotype is not related to molecular events indicating defective DNA repair or EBV infection in these patients. A coherent cause in molecular carcinogenesis with the concomitant RCCs was not proven in this study.

Abstract No 1/8

Intrathyroid thyroglossal duct cyst – case report

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Introduction:
Thyroglossal duct cysts are cystic dilatations of epithelial remnants of the thyroglossal duct tract formed during the migration of the thyroid during embryogenesis. Most patients present as children, although presentation at any age is possible. These congenital lesions present most commonly as midline neck masses at the level of the thyrohyoid membrane and are closely associated with the hyoid bone, but they have been also reported in atypical locations. There have been few reported cases of intrathyroid thyroglossal duct cyst. We report a case of an intrathyroid thyroglossal duct cyst presenting as a painful mass in the lateral neck.

Case report:
A 37-year-old male presented with a painful, left lateral neck mass that was clinically indistinguishable from a thyroid nodule. Ultrasound revealed a cystic lesion of the left thyroid lobe. Findings of ultrasound-guided fine-needle aspiration biopsy were consistent with inflammatory changed cystic lesion. After the antibiotic therapy, the mass was less painful but reduced in size insignificantly. The patient was admitted for the surgical treatment and left thyroid lobectomy was performed. Gross examination of the thyroid lobe revealed a well defined cystic lesion, 2.5 cm in diameter, filled with white to yellow granular content. Microscopically, the cyst wall was partially lined with flattened, nonkeratinizing squamous epithelium. The lining epithelium was, however, mostly desquamated and replaced by the granulation tissue rich in mononuclear inflammatory cells, hystiocytes, macrophages and siderophages. The cyst was completely embedded within the thyroid gland and no tract was found.The surrounding parenchyma consisted of variably sized thyroid follicles lined with normal-looking thyreocytes. The pathological findings were consistent with intrathyroid thyroglossal duct cyst, in this case secondarily changed due to inflammation.

Discussion:
Thyroglossal duct cysts are congenital lesions that usually develop in the midline of the neck. They can be unlined or lined with pseudostratified, ciliated columnar respiratory epithelium or a nonkeratinizing squamous epithelium. Atypical presentations include tongue, suprasternal and thyroid locations. In the review of the literature we found eight reported cases of thyroglossal duct cyst located in the thyroid. These cysts are usually asymptomatic but symptoms can include cough, intermittent choking, shortness of breath or pain due to infection. In this case the patient presented with a painful mass in the lateral neck and findings of ultrasound-guided fine-needle aspiration biopsy were consistent with inflammatory changed cystic lesion. The cytology of the aspirated material was useful in distinguishing the

lesion from other entities such as carcinoma with cystic changes, dermoid cyst, thymic cyst and other cystic lesions. However, final diagnosis was set after the patohistological evaluation of the surgically removed thyroid lobe. This case describes the atypical location of the thyroglossal duct cyst and suggests that intrathyroid thyroglossal duct cyst should be included in the differential diagnosis of patients with cystic thyroid lesions.

Literature:

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Abstract No 1/9

The Cytokine Receptor Superfamily Serves as a Promising Therapeutic Target in Colorectal Cancer – Which Prospects Arise from the Prolactin Receptor?

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Introduction:
Targeted cancer therapy directed against tumor-promoting receptors represents a sophisticated therapeutic approach. The human prolactin receptor (PRLR), a member of the Cytokine Receptor Superfamily, has been reported to promote tumour growth through an auto-/paracrine loop. However, the amount and clinical significance of PRLR expression in colorectal cancer (CRC) remains to be elucidated. Our study aimed to evaluate the prevalence of PRLR in a large sample of CRC and to correlate findings with clinicopathological data as well as patient outcome. In addition, PRLR expression in local and distant metastases was compared with that of corresponding primary tumours.

Methods:
400 patients were randomly sampled from the files of the CRC database of the Institute of Pathology, Medical University of Graz, Austria. Of these, 373 primary CRC and 171 corresponding metastases were evaluated for PRL-R expression by immunohistochemistry using a tissue microarray technique. Follow-up data were available for 342 (91%) patients. Median follow-up was 59 months (mean 64, range 0-182). PRL-R expression was semiquantitatively scored as either focal (<10% of tumour cells positive), moderate (10-50%), or extensive (>50%). PRLR expression was related to various clinicopathological parameters and to patient outcome.

Results:
PRLR expression was observed in 360 (97%) primary tumours, with 21 (6%) cases showing focal, 55 (15%) moderate and 284 (76%) extensive expression, respectively. Extensive PRLR expression was significantly associated with tumour size ($p=0.002$) and grade ($p<0.001$) as well as histological subtype, with classical adenocarcinomas showing stronger PRLR expression than mucinous adenocarcinomas ($p<0.001$). Somer's D coefficients for concordance of primary tumours with corresponding lymph node and distant metastases were $D = 0.719$ ($p<0.001$) and $D = 0.535$ ($p=0.001$), respectively.

Regarding the whole group of tumours, extensive PRL-R expression predicted both disease progression as well as cancer-related death (p=0.08 each). Restricting analysis to high grade cancers, 43/73 (59%) patients with tumours showing extensive PRLR expression experienced disease progression compared with 11/33 (33%) patients with tumours either lacking PRLR expression or showing only focal/moderate expression (p=0.03). Similarly, 39/73 (53%) patients with tumours showing extensive PRL-R expression died of disease compared with 9/33 (27%) patients with tumours either lacking PRLR expression or showing only focal/moderate expression (p=0.04).

Discussion and Conclusion:
PRLR expression is common in CRC, with high concordance between primary tumours and corresponding metastases. Extensive expression was significantly associated with tumour size, grade and histological subtype. In view of evolving targeted therapy strategies in CRC, widespread PRLR expression may offer an additional therapeutic perspective in affected patients.

Abstract No 1/10

Aurora-kinase B expression is dependent on cell proliferation in breast carcinoma

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Introduction:
Chromosomal instability and formation of aneuploidy are key features of the malignant phenotype. Deregulation of the components of the mitotic apparatus may significantly contribute to errors of the cell division and by that, to tumor aggressiveness. Aurora-B (AuB) is a mitotic kinase which acts as a part of the chromosomal passenger complex essential for chromosome segregation. During normal cell cycle the Aurora B kinase is expressed in late G2 and M phase and remains active in the process of mitosis. Overexpression of AuB was reported in different conditions including aggressive lymphomas, breast carcinoma and colorectal carcinoma. However, systemic evaluation of AuB expression in relation to the cell cycle was not performed so far. In our study we addressed this issue by the parallel estimation of the AuB expressing G2/M fraction and the proliferative fraction of breast cancer cases.

Methods:
33 cases of invasive ductal and lobular breast carcinomas were examined immunohistochemically for the AuB and the Mib-1 cell proliferation fraction to define the potential overexpression and increased or delayed effect of the kinase activity in tumor cells. The immunopositive cells were determined semiquantitatively in percentage of the total tumor cell fraction. In addition, chromosome 17 copy number and the Her-2 gene status was also determined by FISH analysis.

Results:
AuB expression was found in the range of 0 to 35 %, (mean=7.7, SD∔10.1) with a subset of breast carcinomas showing highly elevated AuB expression. Cell proliferation capacity (Mib-1 index) of the same tumors was between 1 and 95 % (mean=22.6, SD∔23.6). Interestingly, a strong correlation was found between the AuB and Mib-1 positive fraction (r=0.75), suggesting, that increased expression of AuB is a feature of tumors with high proliferative fractions. Breast carcinomas with Her-2 amplification presented with a significantly elevated AuB fraction (p=0.05) but they also showed higher Mib-1 proliferation index. Discussion and Conclusion: In conclusion, the mitotic kinase AuB is well detectable by immunohistochemistry under routine conditions. The rate of AuB expression proved to be dependent on the proliferative fraction of the tumor. To obtain an accurate picture on AuB overexpression in proliferating cell populations the AuB/MiB-1 index also considering the increase in the G2/M cell fractions in proliferating cell populations is proposed.

Abstract No 2/1

The role of Lim1 in renal development and renal neoplasms

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Introduction:
Lim1 encodes a LIM class homeodomain transcription factor, which plays an important role in the mesenchymal-epithelial transition during kidney development of mouse and rat. Inactivation of *Lim1* in nephric duct tissue leads to development of smaller kidneys, hydronephrosis and hydroureter, indicating abnormal formation of distal ureter.
In our study we investigated the role of *Lim1* during normal human kidney development, cystic renal maldevelopment and different renal neoplasms. We also analysed characteristics of Lim1 further in a cell culture model.

Methods:
Immunohistchemistry was performed on paraffin-embedded samples of fetal kidneys of different gestational ages, multicystic dysplastic kidneys and different renal neoplasms.
Lim1 was overexpressed in HEK-293 cells by transfection of a vector containing the coding sequence of *Lim1.* Changes in gene expression was analysed by qRT-PCR and immunohistochemistry, influence on the cell cycle by FACS analysis.

Results:
In our samples we identified so far expression of Lim1 beginning at 10 weeks of gestation in S-shaped and comma shaped bodies. At a later gestational age some immature glomeruli also showed positivity for Lim1. So far analysis of renal neoplasms revealed expression of Lim1 in some cases of nephroblastomas, but none in renal cell carcinomas. Cell culture experiments so far indicated that overexpression of Lim1 was sufficient to enhance gene expression of an epithelial phenotype.
Discussion and Conclusion: Our study indicates that Lim1 is expressed during human renal development and downregulated in mature kidney. In embryonal tumors of the kidney reactivation can be observed suggesting a possible oncogenic role of this transcription factor.

Abstract No 2/2

Intrauterine fetal death during the 3rd trimenon-impact of placental findings

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Introduction:
Intrauterine fetal death (IUFD) is an immense burden for every person involved. Therefore it is very important to identify the different fetal, maternal and placental causes for IUFD. A better knowledge about the correlation of the risks would make better counselling of parents possible and might prevent such events. In our study we are not only assessing fetal and maternal risk factors, but we also investigate macroscopic and histological findings of the placenta, which cannot be identified on ultrasound.

Methods:
In a retrospective study 65 IUFDs from the 28th week till term were included. Investigated maternal risks are age, BMI, diabetes, hypertension, earlier pregnancies, HELLP, smoking and (pre-) eclampsia. Fetal parameters include weight, ultrasound biometry, twins, umbilical cord complications, quantity of the amniotic fluid and underlying syndromes. Macroscopic and histological findings of the placenta including status of maturation are compared as well.

Results:
So far 13 placentas among all the samples investigated showed inappropriate maturation of chorionic villi compared to gestational age. 10 placentas had a trimmed weight beneath the 10 percentile. 6 placentas had not only delayed maturation of chorionic villi, but also a low placental weight.

Discussion and Conclusion:
So far in the literature maternal risk factors such as hypertension and eclampsia have been widely investigated in different studies, whereas placental morphology as an independent risk factor has not been investigated in detail. Our study indicates that low placental weight and inappropriate maturation might play a role in IUFD.

Abstract No 2/3

The prognostic value of p16 and p27 in recurrent low and high grade bladder cancer

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Introduction:
We investigated the value of expression and distribution pattern of p16, p27 in superficial bladder cancer in correlation with p53, Ki-67 and CK20 and clinical-pathological parameters.

Methods:
Primary and recurrent urothelial carcinomas of 31 patients were evaluated for the expression of p16, p27, Ki67, p53, and CK20 by means of immunohistochemistry. Specimens were analyzed using a scoring system (range 0 – 12) including percentage of positive cells and intensity of staining. In addition the localization of positively stained cells within each tumor was evaluated taking into account the localization of staining in basal, intermediate and/or superficial cells. In addion FISH fpr 9p21(p16) was performed in selceted cases including different p16 expression patterns.

Results:
A total of 107 tumors was analysed. The expression of p16 and p27 correlated significantly with grade ($p<0.001$ and $p=0.02$) as well as with expression of p53 ($p<0.001$ for both) and ki67 ($p=0.02$ and $p<0.001$).
Both, p16 and p27 were mostly found in a patchy distribution. While p16 staining was mainly found in basal and intermediate cell layers, p27 was mostly found in the superficial cell layers. Comparing the expression pattern of different markers, a strong an homogenoeus expression was restricted to high grade tumors, while in low grade tumors a more heterogeneous expression pattern was noted. The recurrent tumors of the patients mostly showed a similar expression pattern than the primary tumor.

Discussion and Conclusion:
p16 and p27 are differentially expressed in low and high grade bladder cancer suggesting an association with the degree of differentiation.

Abstract No 2/4

Distribution of HPV genotypes in penile squamous cell carcinomas

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Background
Penile squamous cell carcinomas (SCC) are either human papilloma virus (HPV) induced or arise in the background of dermatoses. In contrast to carcinomas of the uterine cervix (nearly in 100% HPV-induced) and vulvar SCC (about 30% HPV-induced) the prevalence of HPV and dermatoses in penile SCC is not exactly known.

Material and Methods
We analyzed retrospectively 95 archival penile surgical specimens (28 foreskins, 21 excisions of glans penis and 46 penectomies) from the Institute of Pathology, Medical University Graz, Styria, Austria. 18 in-situ SCC and 77 invasive SCC (TNM 2002: 63/95=66% pT1, 9/95 = 9% pT2, 5/95 = 5% pT3) were analyzed by immunohistochemistry with antibodies to p16 („surrogate marker" for transforming HPV- infection) and 85 of these 95 penile SCC were additionally analyzed with molecular methods for 27 HPV-low risk und HPV high-risk genotypes (Innogenetics LIPA HPV-Genotyping)

Results
65 of 95 (68%) penile SCC were p16-positiv, 30/95 (32%) were p16-negative. All p16-negative SCC were also negative for HPV after genotyping. For 55 of the 65 p16-positive SCC genotype analysis was available: 48/55 SCC (87%) harboured HPV16 genotype as a single genotype and in 2/55 SCC (3.6%) HPV 45 was identified as the single genotype. HPV 18 was not identified as a single genotype, but present in 2/5 SCC with multiple HPV-high risk genotypes. In total, only 5/55 (9%) SCC harboured more than one HPV genotypes: in 2 SCC HPV-18 was detected together with HPV 31 and 58, and 3 SCC HPV 31, 33, 51 and 66.

Conclusions
30% of penile SCC are HPV-negative and associated with lichen sclerosus or lichen planus. About 2/3 of the examined penile SCC in Styria are HPV-induced and in over 90% HPV16 is the sole genotype. HPV18 was not detected as a single HPV-genotype in penile SCC, only in infections with multiple HPV-high-risk and low-risk genotypes. The prevalence of HPV in penile SCC is higher than in vulvar SCC but lower than in cervical uterine carcinomas. HPV-vaccination could prevent a significant percentage of penile SCC.

Abstract No 2/5

Nephrogenic rests – genetic precursor lesions of nephroblastomas?

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Introduction:
Nephroblastomas are embryonal renal neoplasms. Currently nephrogenic rests are considered as precursor lesions of nephroblastomas. In our study we investigated the genetic relationship between intralobar nephrogenic rests and nephroblastomas comparing genetic changes by array CGH.

Methods:
Manual microdissection was performed to isolate blastemal and epithelial regions of nephroblastomas and nephrogenic rests. 250ng genomic DNA and reference DNA were differentially labelled with dCTP-Cy5 and dCTP-Cy3, respectively and co-hybridized on a 8x60 K array platform. Slides were scanned using Agilent's microarray scanner G2505B and analyzed using Agilent DNA Analytics software 4.0.76.

Results:
Analysis of 7 nephroblastomas and 9 nephrogenic rests revealed partial gains of chromosome 1, chromosome 12, chromosome 16 and chromosome 17 in nephroblastomas. There was no difference in genetic aberrations between blastemal and epithelial regions. Nephrogenic rests also showed gains of the same chromosomal regions in the identical chromosomes, additionally, gains of chromosome 22 and partial deletions of chromosomes 13 and 16.

Discussion and Conclusion:
Our data demonstrate, as already described for perilobar nephrogenic rests, additional genetic changes in intralobar nephrogenic rests compared to corresponding nephroblastomas. These results indicate that oncogenic transformation might not apply to all nephrogenic rests.

Abstract No 2/6

Six2 – embryonically active transcription factor with oncogenic properties?

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Introduction:
The morphology of nephroblastomas recapitulates embryonal kidney development. Comparison of gene expression patterns of fetal kidney and primary nephroblastomas indicated that blastema is in the stage of mesenchymal-epithelial transition. During kidney development metanephric mesenchyme also contains a renal progenitor cell population expressing Six2. In our study we investigated whether blastema shows not only morphological but also genetical characteristics of progenitor kidney cells possibly influencing prognosis and treatment options.

Methods:
Manual microdissection was carried out to separate morphologically distinct tumor areas of nephroblastomas. Up to 500 ng of total RNA were reverse transcribed into cDNA using the High Capacity cDNA reverse transcription kit (Applied Biosystems, UK). QRT-PCR was performed to analyse the mRNA expression of the Six2 gene relative to the housekeeping gene 18S.

Results:
So far we analyzed samples of blastemal and epithelial areas from nephroblastomas with various morphological subtypes. Blastemal regions showed a high level of mRNA expression of Six2 in all cases of blastema rich tumors and 2 cases with mixed phenotype. One triphasic mixed tumor showed relatively similar expression in both epithelial and blastemal regions. However, all epithelial regions investigated so far had low expression of six2 compared to blastema.

Discussion and Conclusion:
Our study shows that epithelial and blastemal areas even within the same tumor harbour a different genetic pattern. This might contribute to the divergent response to chemotherapy and clinical course.

Abstract No 2/7

Expression of ATGL is up-regulated in malignant tumors under hypoxic conditions

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Introduction:
Lipid metabolism is established as a key factor in the pathophysiology of malignant growth. Under hypoxic conditions, malignant cells detoxify excess non-oxidized free fatty acids (FFA) via esterification into triglycerides (TG). Since adipose triglyceride lipase (ATGL) is the key enzyme for subsequent remobilization, we evaluated its role under hypoxic conditions.
Methods: HT29 (adenocarcinoma, colon), HepG2 (hepatocellular carcinoma), U87-MG (glioblastoma) and HTB115 (leiomyosarcoma) cells were cultured under normoxic (20%) or hypoxic (1% oxygen) conditions in the presence or absence of Xanthohumol (XN), a diacylglycerol acyltransferse inhibitor. Lipids were analyzed by mass spectrometry. ATGL and hormone-sensitive lipase (HSL) mRNA were determined by RT-PCR, protein by immunohistochemistry and lipase activity by FFA release from TG.

Results:
Under hypoxic conditions, ATGL mRNA expression was up-regulated in all the four cell lines up to 2.1-fold. Increased levels of ATGL protein were detected in HTB115 cells. However, there was no significant increase in lipase activity. Interestingly, we detected an increase in cytoplasmic TG (72%), but a decrease in diacylglycerol levels under hypoxia (64%) in HTB115 cells. HSL mRNA levels showed no significant differences between normoxia and hypoxia in all cell lines. Importantly, cells treated with XN had no increase in ATGL mRNA and showed decreased proliferation and increased cell death.

Discussion and Conclusion:
Up-regulation of ATGL on mRNA and protein level might be a consequence of TG accumulation in malignant cells under hypoxic conditions. Why this up-regulation is not accompanied by increased lipase activity resulting in TG conversion to DAG and FAA is currently being investigated. These mechanisms might indicate an important role for ATGL in the metabolism of malignant cells facilitating survival in a hostile environment.

Abstract No 2/8

Dermatofibroma, a neoplastic or an inflammatory lesion?

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Introduction:
Dermatofibroma (DF) is a frequent skin lesion which is often easily recognised clinically and histologically. However, the theory about the nature of DF is still not officially accepted.
Langerhans cells (LC) are antigen-presenting cells that are, when compared to normal skin, more numerous in a spectrum of inflammatory skin lesion and less numerous in malignant tumours. The results are not so straightforward for benign tumours so we tried to see if the number of LC in DF points more toward inflammatory or neoplastic lesion.

Methods:
From our archive we collected 20 skin biopsies from each leasion (postoperative scar, dermatofibroma and dermatofibrosarcomas) and retrospectively analyse them. We compared the number of intraepidermal LC over DF with the number of intraepidermal LC over scar and over DFS. For highlighting the LC in the epidermis CD1a antibody (clone OB-2; Dako, Glostrup, Denmark) were used. The intraepidermal CD1a+ cells were enumerated as a percentage of 100 epidermal cells. At least two areas on high power field were counted and mean +/- SD percentage was calculated in each specimen. Statistical analysis was preformed by nonparametric Mann-Whitney U test. Differences were considered to be significant at $p<0.05$.

Results:
The number of intraepidermal LC above DF was found to be significantly lower than the number of LC in the epidermis above the scar (2.00+/-0.52 and 6.80+/-1.89; $p<0.001$). We also found significantly smaller number of intraepidermal LC in DFS when compared to the number of intraepidermal LC in a scar (2.76+/-1.18 and 6.64+/-1.86; $p<0.001$). There was no statistically significant difference between the number of intraepidermal LC in DF and DFS (2.00+/-0.52 and 2.76+/-1.18; $p=0.056$).

Discussion and Conclusion:
We used DFS as an example of neoplastic lesion and scar as a model for final phase inflammatory lesion. Both lesions are morphologicaly similar to DF. The number of intraepidermal LC in DF is closer to the number of intradermal LC in DFS than to the scar. Based on the number of LC, DF is closely related to a neoplastic origin than to inflammatory reaction.

Abstract No 2/9

Solid pseudopapillary tumors of the pancreas: a case series, comparison of histopathological and clinical data

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Introduction:
Solid pseudopapillary neoplasms (SPN) are rare pancreatic tumors, representing only 1% to 2% of all pancreatic neoplasms, first described by Frantz in 1959. Frantz described three patients suffering from SPN, with solid and cystic components that were previously clinically misdiagnosed as nonfunctioning islet cell tumors. The fact that the tumor occurs predominantly in young women suggests that gender specific factors may play a role, although it has also been reported in older and male patients. However, no concomitant data has been found until now.

Methods:
The clinical course, pathohistological data and clinical outcome of four patients with SPN treated at Ruhr-Universität Bochum were described. Furthermore additional immunohistochemical and molecularbiological data is presented.

Results:
From 2008 to 2009 four patients with SPN were diagnosed at our institution. Among others, this case series includes three female (age range 17-56 years) and one male patients (26 years). Predominantly the tumors were localized in the corpus (one in the head, two in the corpus and one in the tail of pancreas), with a mean diameter of 3,6cm. All tumors exhibited K-ras wildtype. Immunohistochemistry including DPC4, β-catenin, progesterone-receptor and synaptophysin was analysed, too.

Discussion and Conclusion:
SPN are rare pancreatic neoplasms with low malignant potential found primarily in young women. Curative surgical resection may be performed safely to rule out malignancy. After complete resection of the tumor the prognosis is excellent. However preoperative diagnosis is difficult and cytological diagnosis is impossible. Histopathologically the SPN should be sepsrsted from endocrine tumors and acinar carcinoma.

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Der Goldstandard in der HER2-Diagnostik ist die Pathologie - die Qualität Ihrer Arbeit entscheidet

Weisgerber[1] et al. untersuchten den prognostizierten jährlichen Rückgang an PatientInnen mit metastasiertem Mammakarzinom in 5 EU-Ländern (F, G, I, E, UK) nach adjuvanter Therapie mit Herceptin®:

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- → verringert die Häufigkeit des metastasierten Mammakarzinoms
- → kann die Mammakarzinom-Mortalitätsrate senken

1 Weisgerber et al., ASCO 2008, Poster 6589 zusammen mit geeigneten Screening-Massnahmen
2 Weisgerber et al., ASCO 2008, Poster 6589

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1 De Matteo, R et al. Adjuvant imatinib mesylate after resection of localised, primary GIST: a randomised, double blind, placebocontrolled trial. The Lancet 2009; 373: 1097-1104 | 2 Austria Codex Fachinformation Glivec®

FACHKURZINFORMATION: Bezeichnung des Arzneimittels: Glivec 100 mg Filmtabletten, Glivec 400 mg Filmtabletten; **Qualitative und Quantitative Zusammensetzung:** Jede Filmtablette enthält 100 mg (400 mg) Imatinib (als Mesilat). **Liste der sonstigen Bestandteile:** Kern: Mikrokristalline Cellulose, Crospovidon, Hypromellose, Magnesiumstearat, hochdisperses Siliciumdioxid. Film: Eisen (III)-oxid (E 172), Eisenoxydhydrat x H_2O (E 172), Macrogol, Talkum, Hypromellose. **Anwendungsgebiete:** Glivec ist angezeigt zur Behandlung von • Erwachsenen und Kindern mit neu diagnostizierter Philadelphia-Chromosom (bcr-abl)-positiver (Ph+) chronischer myeloischer Leukämie (CML), für die eine Knochenmarktransplantation als Erstbehandlungsmöglichkeit nicht in Betracht gezogen wird • Erwachsenen und Kindern mit Ph+-CML in der chronischen Phase nach Versagen einer Interferon-Alpha-Therapie, in der akzelerierten Phase oder in der Blastenkrise • Erwachsenen mit neu diagnostizierter Philadelphia-Chromosom-positiver akuter lymphatischer Leukämie (Ph+ ALL) in Kombination mit einer Chemotherapie • Erwachsenen mit rezidivierter oder refraktärer Ph+ ALL als Monotherapie • Erwachsenen mit myelodysplastischen/myeloproliferativen Erkrankungen (MDS/MPD) in Verbindung mit Genumlagerungen des PDGF-Rezeptors (platelet-derived growth factor) • Erwachsenen mit fortgeschrittenem hypereosinophilem Syndrom (HES) und/oder chronischer eosinophiler Leukämie (CEL) mit FIP1L1-PDGFRα-Umlagerung. Die Wirkung von Glivec auf das Ergebnis einer Knochenmarktransplantation wurde nicht untersucht. Glivec angezeigt zur • Behandlung c-Kit-(CD 117)-positiver nicht resezierbarer und/oder metastasierter maligner gastrointestinaler Stromatumoren (GIST) bei Erwachsenen • adjuvanten Behandlung Erwachsener mit signifikantem Risiko eines Rezidivs nach Resektion c-Kit-(CD 117)-positiver GIST. Patienten mit einem niedrigen oder sehr niedrigen Rezidivrisiko sollten keine adjuvante Behandlung erhalten • Behandlung Erwachsener mit nicht resezierbarem Dermatofibrosarcoma protuberans (DFSP) und Erwachsener mit rezidivierendem und/oder metastasiertem DFSP, die für eine chirurgische Behandlung nicht in Frage kommen. Bei Erwachsenen und Kindern mit CML basiert die Wirksamkeit von Glivec auf den hämatologischen und zytogenetischen Gesamtansprechraten und auf dem progressionsfreien Überleben, bei Ph+ ALL und MDS/MPD auf den hämatologischen und zytogenetischen Gesamtansprechraten, bei HES/CEL auf der hämatologischen Ansprechrate, bei nicht resezierbaren und/oder metastasierten GIST und DFSP auf den objektiven Ansprechraten und bei adjuvanter Behandlung der GIST auf dem rezidivfreien Überleben. Die Erfahrung mit der Anwendung von Glivec bei Patienten mit MDS/MPD in Verbindung mit PDGFR-Genumlagerungen ist sehr begrenzt (siehe Abschnitt 5.1). Außer für neu diagnostizierte CML in der chronischen Phase liegen keine kontrollierten Studien vor, die einen klinischen Vorteil oder ein verlängertes Überleben bei diesen Erkrankungen belegen. **Gegenanzeigen:** Überempfindlichkeit gegen den Wirkstoff oder einen der sonstigen Bestandteile. **Inhaber der Zulassung:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB,Vereinigtes Königreich; **Abgabe:** NR, apothekenpflichtig. **Pharmakotherapeutische Gruppe:** Protein-Tyrosinkinase-Inhibitor; ATC-Code: L01XE01. Weitere Informationen betreffend Warnhinweise und Vorsichtsmaßnahmen für die Anwendung, Wechselwirkung mit anderen Mitteln, Nebenwirkungen und Gewöhnungseffekte sind der veröffentlichten Fachinformation zu entnehmen.