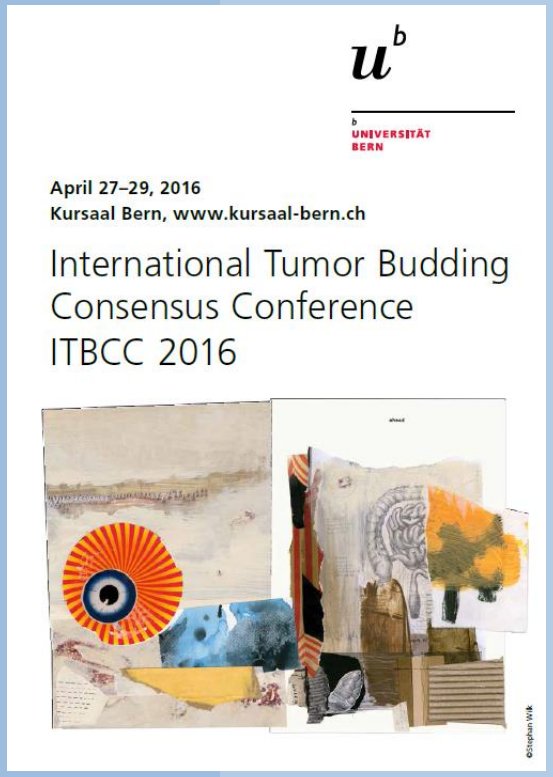
UNIVERSITÄT BERN

Endlich „Budding – Konsensus“-Ergebnisse der ITBCC 2016

Dr. med. Heather Dawson
Institut für Pathologie
Universität Bern



Kloster Banz, 24. Juni 2017

Übersicht

UNIVERSITÄT BERN

Hintergrund

Tumor Budding: Biologie und Anwendungsmöglichkeiten

ITBCC 2016

Zusammenfassung

Was ist Tumor Budding?

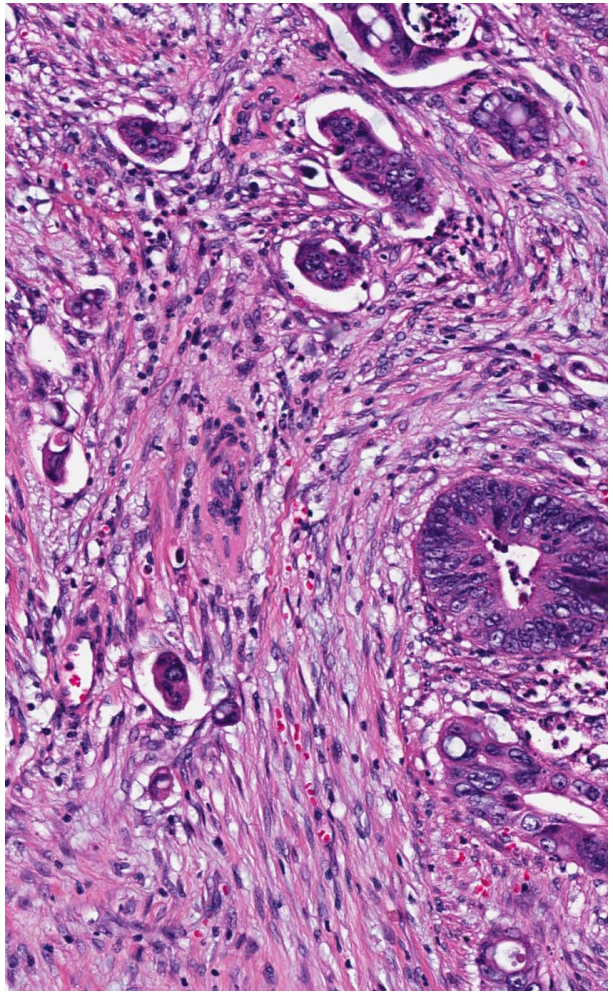
UNIVERSITÄT BERN

Definition
Tumoreinzelzellen und kleine Tumorzellgruppen an der invasiven Front des kolorektalen Karzinoms (peritumorale Buds, PTB)
Jass et al, JCP 2003

Auch im Zentrum des Tumors (intratumorale Buds, ITB)
Zlobec et al, Br J Cancer 2014

Erstmals in den 1950ern beschrieben ('Sprouting')
Imai, Fukuoka Igaku Zasshi 1954

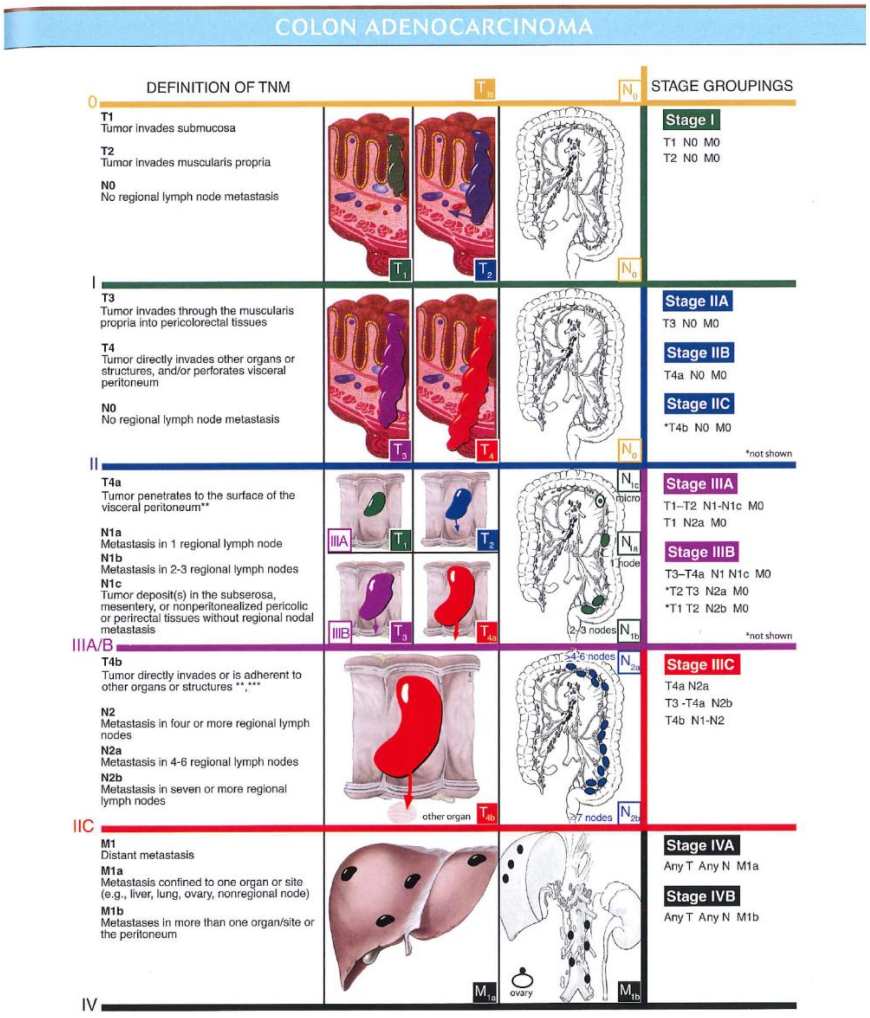
Assoziiert mit L, V, Pn, G, pN, pM und schlechterem Überleben

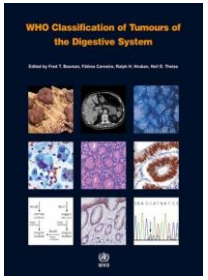


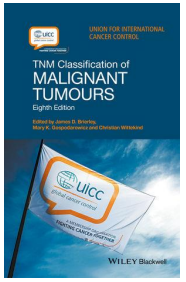
Staging des kolorektalen Karzinoms

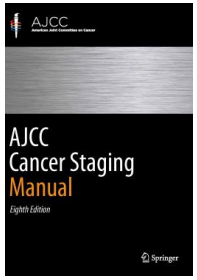
TNM und Prognose

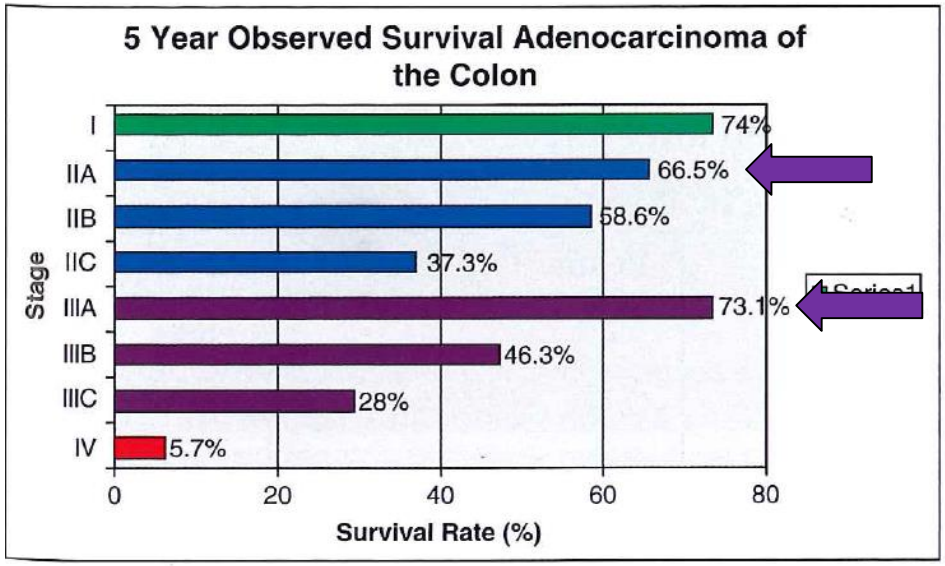
UNIVERSITÄT BERN





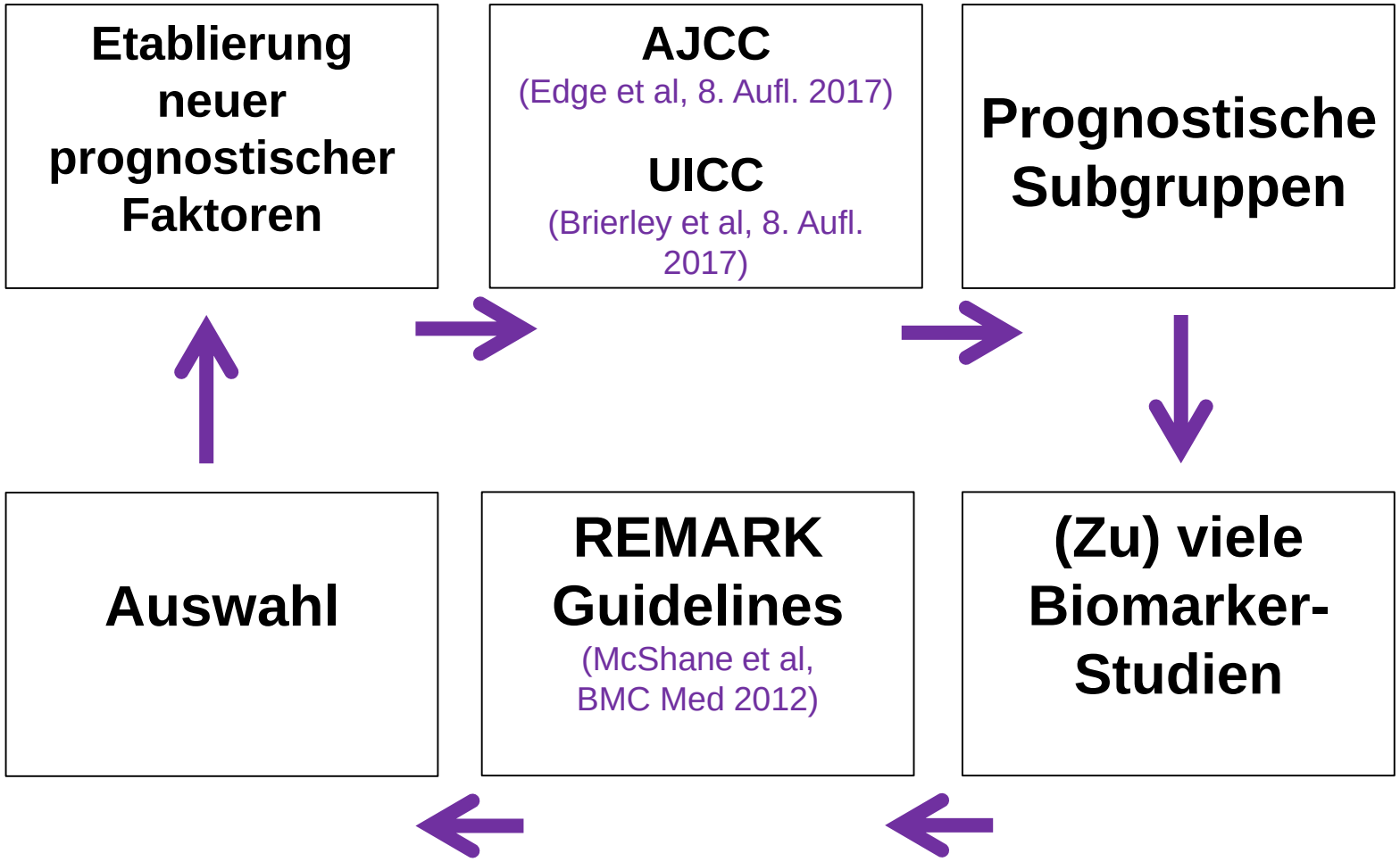






Rubin & Hansen, TNM Staging Atlas 2012; AJCC Cancer Staging Manual, 8te Aufl. 2017; UICC, TNM 8te Aufl. 2017

Entwicklung neuer Biomarker



OPEN ACCESS Freely available online

PLOS MEDICINE

Guidelines and Guidance

Reporting Recommendations for Tumor Marker Prognostic Studies (REMARK): Explanation and Elaboration

Douglas G. Altman[1]*, Lisa M. McShane[2], Willi Sauerbrei[3], Sheila E. Taube[4]

b UNIVERSITÄT BERN

Table 1. The REMARK checklist [1–7].

INTRODUCTION	
1	State the marker examined, the study objectives, and any pre-specified hypotheses.
MATERIALS AND METHODS	
Patients	
2	Describe the characteristics (for example, disease stage or co-morbidities) of the study patients, including their source and inclusion and exclusion criteria.
3	Describe treatments received and how chosen (for example, randomized or rule-based).
Specimen characteristics	
4	Describe type of biological material used (including control samples) and methods of preservation and storage.
Assay methods	
5	Specify the assay method used and provide (or reference) a detailed protocol, including specific reagents or kits used, quality control procedures, reproducibility assessments, quantitation methods, and scoring and reporting protocols. Specify whether and how assays were performed blinded to the study endpoint.
Study design	
6	State the method of case selection, including whether prospective or retrospective and whether stratification or matching (for example, by stage of disease or age) was used. Specify the time period from which cases were taken, the end of the follow-up period, and the median follow-up time.
7	Precisely define all clinical endpoints examined.
8	List all candidate variables initially examined or considered for inclusion in models.
9	Give rationale for sample size; if the study was designed to detect a specified effect size, give the target power and effect size.
Statistical analysis methods	
10	Specify all statistical methods, including details of any variable selection procedures and other model-building issues, how model assumptions were verified, and how missing data were handled.
11	Clarify how marker values were handled in the analyses; if relevant, describe methods used for cutpoint determination.
RESULTS	
Data	
12	Describe the flow of patients through the study, including the number of patients included in each stage of the analysis (a diagram may be helpful) and reasons for dropout. Specifically, both overall and for each subgroup extensively examined report the number of patients and the number of events.
13	Report distributions of basic demographic characteristics (at least age and sex), standard (disease-specific) prognostic variables, and tumor marker, including numbers of missing values.
Analysis and presentation	
14	Show the relation of the marker to standard prognostic variables.
15	Present univariable analyses showing the relation between the marker and outcome, with the estimated effect (for example, hazard ratio and survival probability). Preferably provide similar analyses for all other variables being analyzed. For the effect of a tumor marker on a time-to-event outcome, a Kaplan-Meier plot is recommended.
16	For key multivariable analyses, report estimated effects (for example, hazard ratio) with confidence intervals for the marker and, at least for the final model, all other variables in the model.
17	Among reported results, provide estimated effects with confidence intervals from an analysis in which the marker and standard prognostic variables are included, regardless of their statistical significance.
18	If done, report results of further investigations, such as checking assumptions, sensitivity analyses, and internal validation.
DISCUSSION	
19	Interpret the results in the context of the pre-specified hypotheses and other relevant studies; include a discussion of limitations of the study.
20	Discuss implications for future research and clinical value.

Voraussetzungen für Tumormarker

Qualitätssicherung der Studien

Prognostisch/Prädiktiv

Reproduzierbar

Kosteneffektiv

Tumor Budding beim kolorektalen Karzinom: Ein morphologischer Biomarker für die Praxis?

Douglas et al, PLOS Med 2012

Übersicht

UNIVERSITÄT BERN

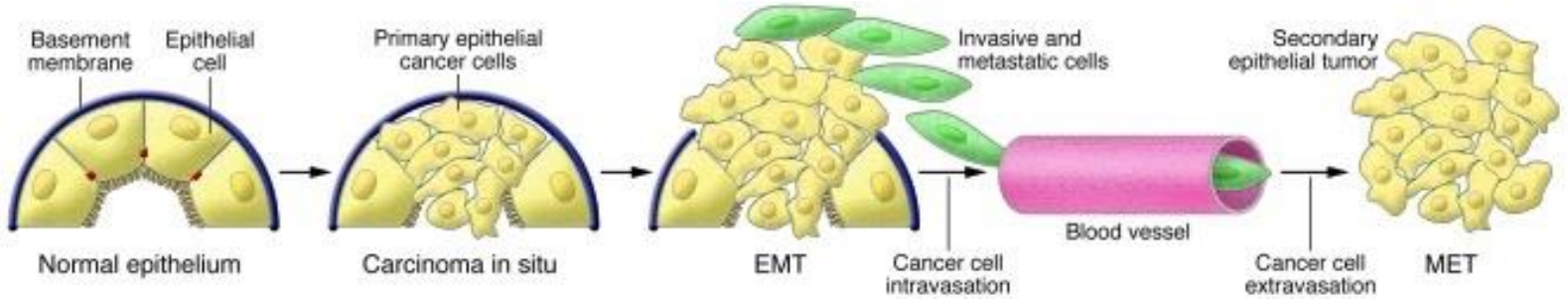
Hintergrund

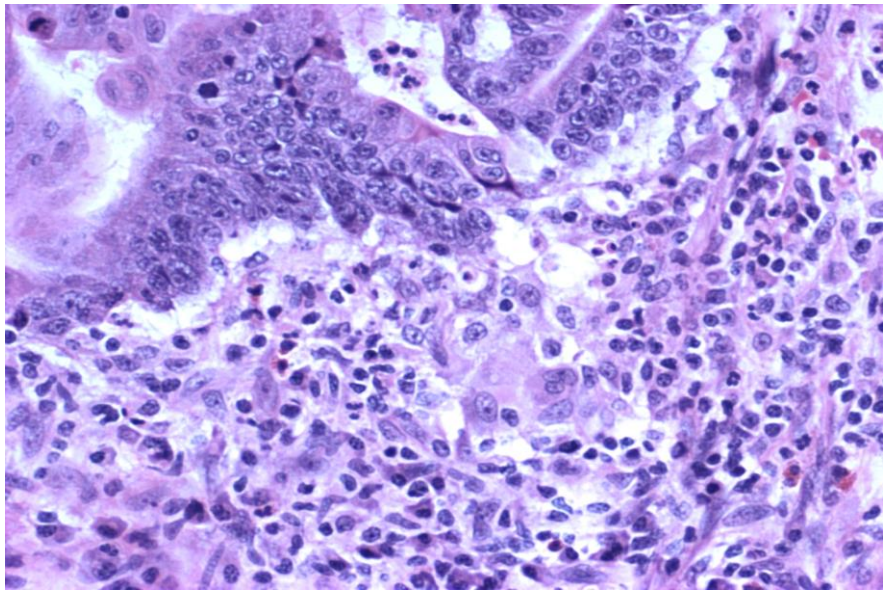
Tumor Budding: Biologie und Anwendungsmöglichkeiten

ITBCC 2016

Zusammenfassung

Epitheliale-mesenchymale Transition

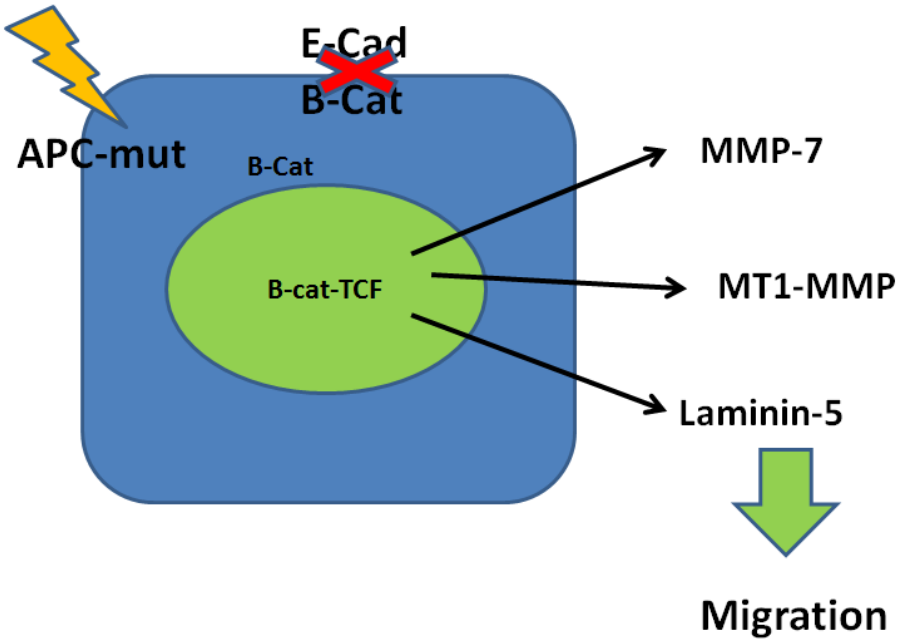


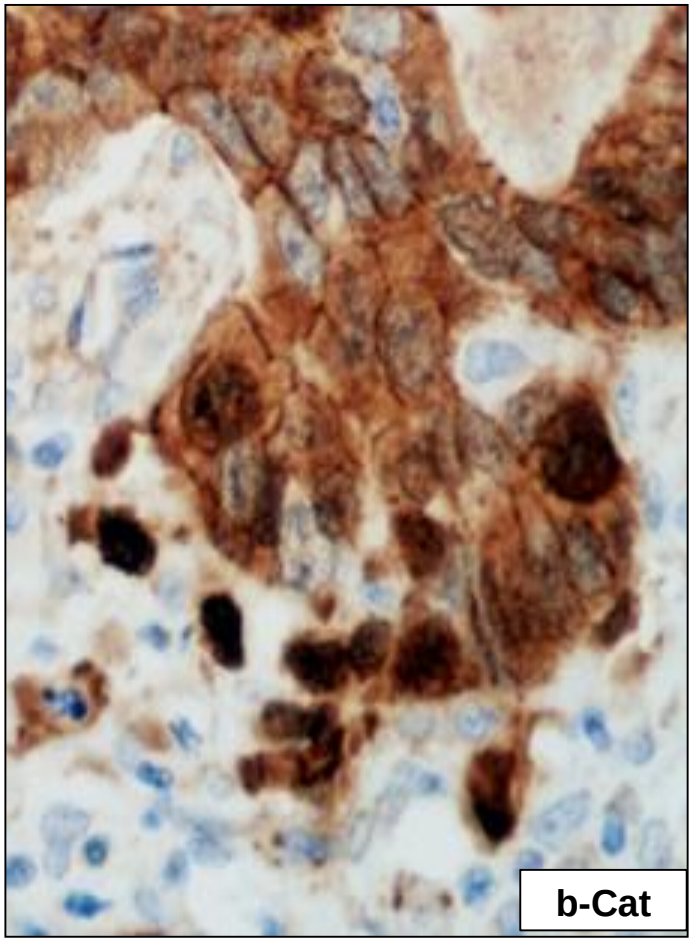


Sind Tumor Buds das morphologische Korrelat?

Kalluri und Weinberg, J Clin Invest 2009

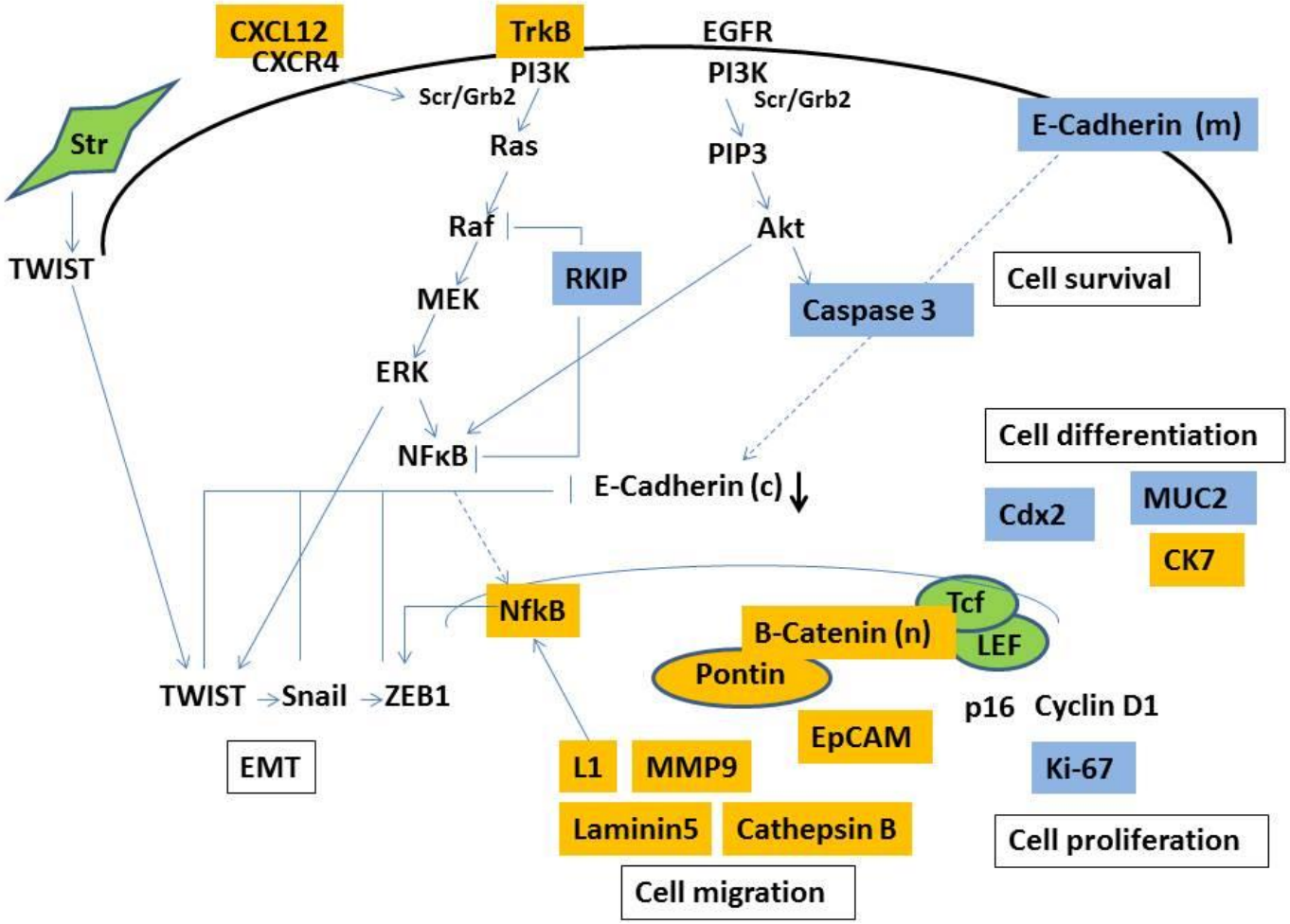
Entstehung von Tumor Buds





Tumor Buds

Proteinexpression

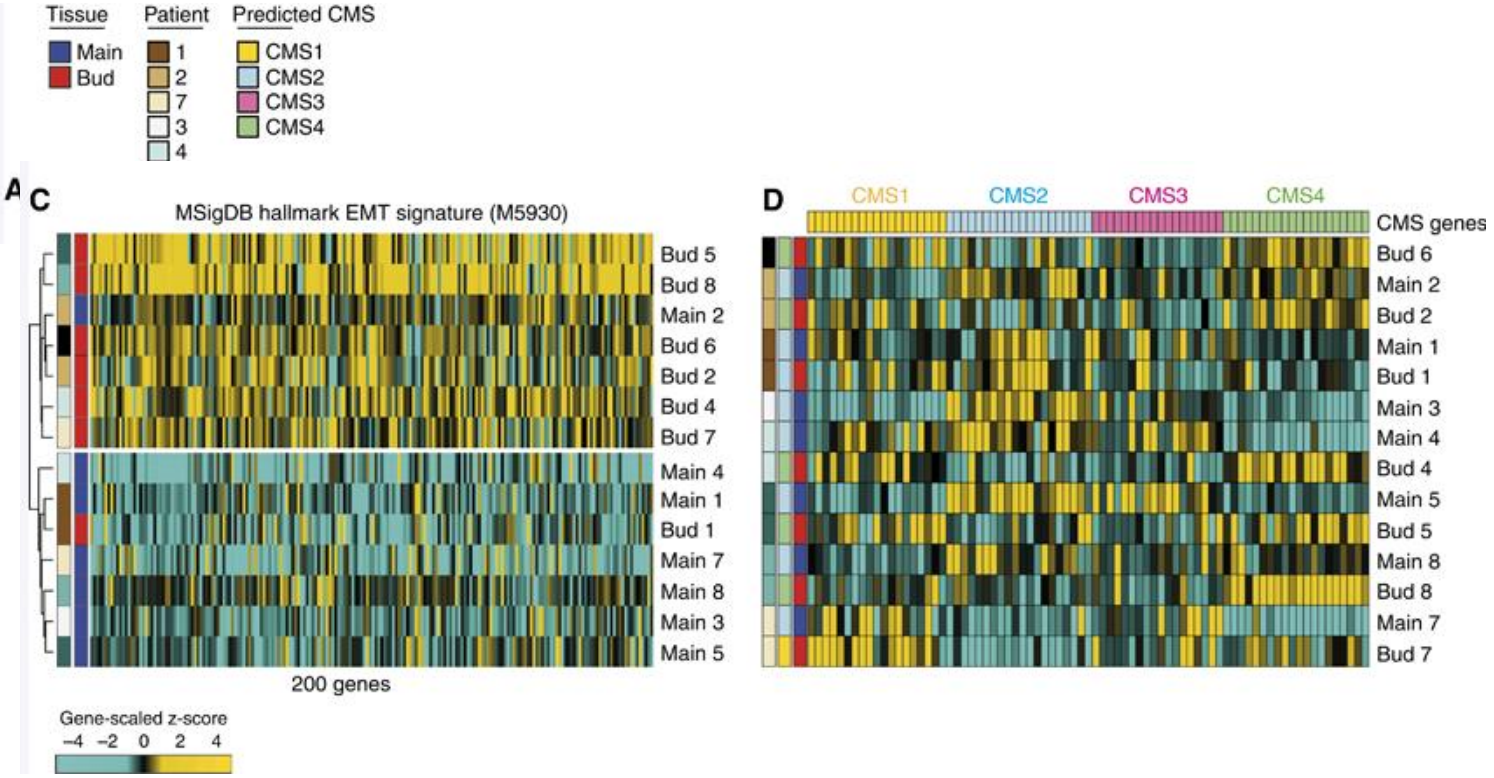


Tumor Buds

EMT auf RNA-Ebene

UNIVERSITÄT BERN

CMS1 MSI Immune	CMS2 Canonical	CMS3 Metabolic	CMS4 Mesenchymal
14%	37%	13%	23%



8 CRC Fälle

Budding-Anteile EMT+, Haupttumor EMT–

CMS switch (CMS2 → CMS4)

Guinney et al, Nat Rev 2015; De Smedt et al, Br J Cancer 2017

Tumor Budding

Als Marker der Tumorprogression

UNIVERSITÄT BERN

Assoziationen:

- Lymph- und Blutgefässinvasion (L und V Stadium)
- Lymphknotenmetastasen (N Stadium)
- Fernmetastasen (M Stadium)
- Unabhängiger ungünstiger Prognosefaktor

Auserwählte Referenzen:

Okuyama et al, J Surg Oncol 2003

Ueno et al, Gastroenterology 2004

Nakamura et al, Dis Colon Rectum 2008

Wang et al, Am J Surg Pathol 2009

Karamitopoulou et al, Mod Pathol 2013

Hase et al, Dis Colon Rectum 1993

Tateishi et al, Mod Pathol 2010

Choi et al, Int J Colorect Dis 2007

Graham et al, Am J Surg Path 2015

Tumor Budding

Klinisch relevante Szenarien

UNIVERSITÄT BERN

Endoskopisch resezierte pT1-Karzinome

Riskofaktor für Lymphknotenmetastasen

→ **Resektion**

Stage II CRC

Indikator für aggressive Tumorbiologie

→ **Adjuvante Therapie**

Prä-operative Biopsien

Marker der Tumorprogression und prädiktiver Wert für Ansprechen auf neoadjuvante Therapie

→ **Neoadjuvante Therapie**

Tumor budding
Klassifikationsysteme und Richtlinien

UNIVERSITÄT BERN

WHO Classification of Tumours of the Digestive System 2010
Bosman, Carneiro, Hruban, Theise
Tumor budding und tumor border configuration nicht integriert in TNM Staging des kolorektalen Karzinoms

UICC Prognostic Factors in Cancer 2006
Gospodarowicz, O'Sullivan, Sobin
Tumor budding: Zusätzlicher Prognosefaktor

AJCC Cancer Staging Manual 2010
Tumor budding: Nicht erwähnt

CAP Protocol for the Examination of Specimens From Patients With Primary Carcinoma of the Colon and Rectum 2016
Tumor budding: Nicht erwähnt

Royal College of Pathologists 2014
Tumor budding: Erwähnt, aber nicht empfohlen

JCSSR (Japan)
Tumor budding obligat beim pT1 CRC

Problem: Keine standardisierte Auswertungsmethode

Übersicht

UNIVERSITÄT BERN

Hintergrund

Tumor Budding: Biologie und Anwendungsmöglichkeiten

ITBCC 2016

Zusammenfassung

ITBCC 2016

Teilnehmer und Ziele

UNIVERSITÄT BERN

Steering Committee

Prof. Gieri Cathomas, MD
Institute of Pathology
Community Hospital Liestal
Switzerland

Dr. Heather Dawson, MD
Institute of Pathology
University of Bern
Switzerland

Prof. Richard Kirsch, MD
Department of Laboratory
Medicine and Pathobiology
Mount Sinai Hospital
University of Toronto
Canada

Prof. Alessandro Lugli, MD
Institute of Pathology
University of Bern
Switzerland

Prof. Robert Riddell, MD
Department of Laboratory
Medicine and Pathobiology
Mount Sinai Hospital
University of Toronto
Canada

Prof. Inti Zlobec, PhD
Institute of Pathology
University of Bern
Switzerland

Participants

Ajioka Yoichi	Japan
Bosman Fred	Netherlands
Cathomas Gieri	Switzerland
Dawson Heather	Switzerland
El Zimaity Hala	Canada
Fléjou Jean-François	France
Hansen Tine Plato	Denmark
Hartmann Arndt	Germany
Kakar Sanjay	USA
Kirsch Richard	Canada
Langner Cord	Austria
Lugli Alessandro	Switzerland
Nagtegaal Iris	Netherlands
Puppa Giacomo	Switzerland
Quirke Phil	UK
Riddell Robert	Canada
Risio Mauro	Italy
Ristimäki Ari	Finland
Sheahan Kieran	Ireland
Smyrk Thomas	USA
Sugihara Kenichi	Japan
Terris Benoit	France
Ueno Hideki	Japan
Vieth Michael	Germany
Zlobec Inti	Switzerland

27.-29.4.2016
22-23 Teilnehmer
Ziel: Evidenz-basierter international standardisierte Richtlinen

ITBCC Bern 2016
Offene Fragen

UNIVERSITÄT BERN

- Was ist ein Tumor Bud?

- Wann ist Tumor Budding klinisch relevant? Datenlage?

- Wird Tumor Budding am HE oder mittels IHC ausgewertet?

- Wo im Tumor wird das Budding gezählt?

- Welche Grösse und Anzahl der Gesichtsfelder?

- Wie wird Tumor Budding rapportiert? Kategorie (cut-off) oder Zahl (kontinuierlich)?

ITBCC Bern 2016
GRADE Richtlinien

UNIVERSITÄT BERN

ELSEVIER

Journal of Clinical Epidemiology 64 (2011) 383–394

Journal of Clinical Epidemiology

GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables

Gordon Guyatt[a,b,*], Andrew D. Oxman[c], Elie A. Akl[m], Regina Kunz[d], Gunn Vist[c], Jan Brozek[a], Susan Norris[e], Yngve Falck-Ytter[f], Paul Glasziou[g], Hans deBeer[h], Roman Jaeschke[b], David Rind[i], Joerg Meerpohl[j,k], Philipp Dahm[l], Holger J. Schünemann[a,b]

[a]*Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario L8N 3Z5, Canada*
[b]*Department of Medicine, McMaster University, Hamilton, Ontario L8N 3Z5, Canada*
[c]*Norwegian Knowledge Centre for the Health Services, St. Olavs plass, 0130 Oslo, Norway*
[d]*Academy of Swiss Insurance Medicine, University Hospital Basel, Basel, Switzerland*
[e]*Department of Medical Informatics and Clinical Epidemiology, Oregon Health and Science University, Portland, OR 97239-3098, USA*
[f]*Division of Gastroenterology, Case and VA Medical Center, Case Western Reserve University, Cleveland, OH 44106, USA*
[g]*Bond University, Gold Coast, Australia*
[h]*Dutch Association of Nursing-home Specialists, Mercatorlaan 1200, 3528 BL Utrecht, The Netherlands*
[i]*Harvard Medical School, UpToDate, Boston, MA, USA*
[j]*German Cochrane Center, Institute of Medical Biometry and Medical Informatics, University Medical Center Freiburg, 79104 Freiburg, Germany*
[k]*Department of Pediatric and Adolescent Medicine, Division of Pediatric Hematology and Oncology, University Medical Center Freiburg, 79106 Freiburg, Germany*
[l]*Department of Urology, University of Florida, College of Medicine, Gainesville, FL 3210, USA*
[m]*Department of Medicine, State University of New York at Buffalo, Buffalo, NY, USA*

Accepted 8 April 2010

9 Sessions, vorgefasste Statements

7 Präsentationen

7 Zusammenfassungen

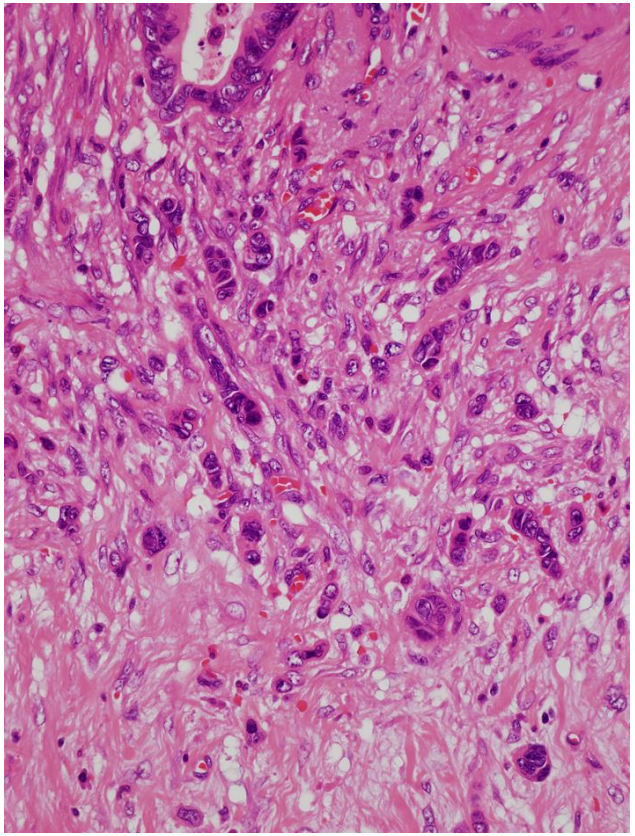
Literatur / e-book

Session Highlights: Session 1

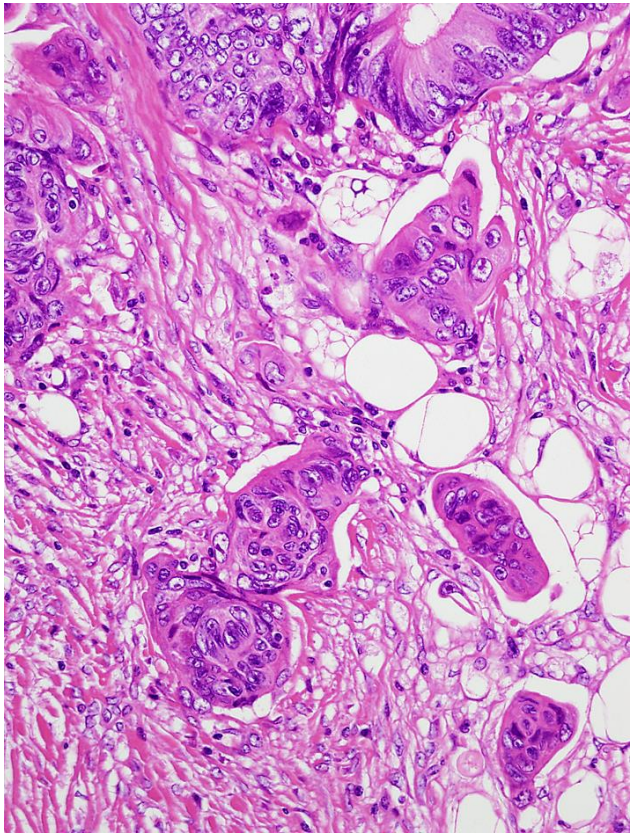
Was ist ein Tumor Bud?

UNIVERSITÄT BERN

Tumor Bud
Tumoreinzelzelle - <5 Tumorzellen
(Ueno H, et al: Histopathology 2002)



Poorly Differentiated Cluster
≥5 Tumorzellen
(Ueno H, et al: Am J Surg Pathol 2012)

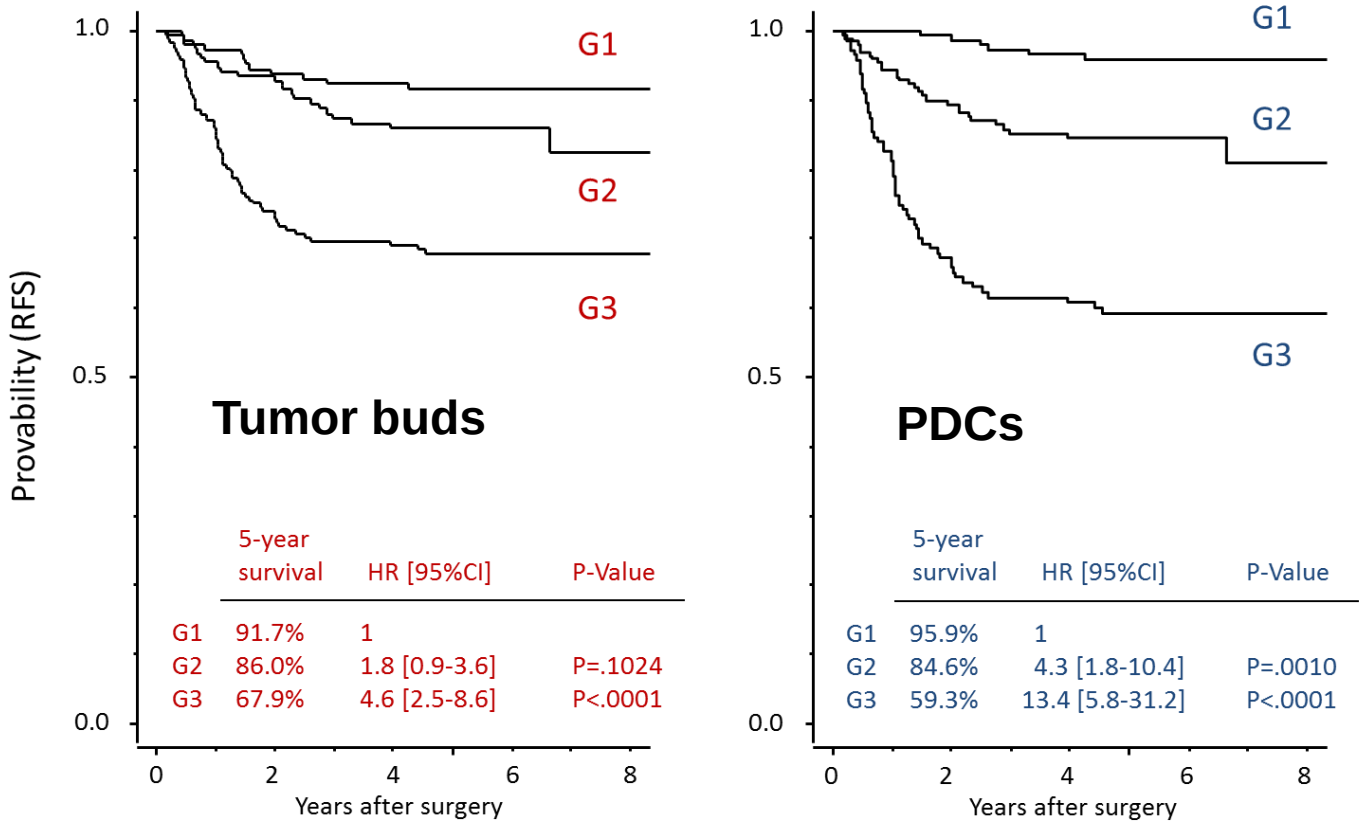


Session 1
Was ist ein Tumor Bud?

UNIVERSITÄT BERN

Single institutional study (NDMC) Stage II, III N=500 cases (2000-05)

Recurrence-free survival



Hideki Ueno, Japan; Ueno et al, Am J Surg Pathol 2012

Session 2: Klinische Szenarien?

Datenlage Tumor Budding beim pT1 CRC

UNIVERSITÄT BERN

Relevanz: Lymphknotenmetastasen → Segmentresektion

- 40 retrospektive Kohortenstudien (zusammen >8000 Patienten)
    - 3 grosse multizentrische Studien (800+ Patienten, alle JPN)
    - Signifikante Assoziation LN+ 38/40 Studien, unabhängig in 25/33 Studien

- 4 Meta-Analysen (2013-2015)
    - OR für LN+ 4.59-7.74
    - Effect size (Beaton et al, Endoscopy 2013): Vergleichbar mit Invasionstiefe und L1

GRADE-Evidenz: Hoch

Session 2: Klinische Szenarien?

Datenlage Tumor Budding beim Stadium II CRC

UNIVERSITÄT BERN

Relevanz: Prognostischer (und prädiktiver?) Faktor → CTX

- 9 retrospektive Kohortenstudien (zusammen > 1200 Patienten)

  - Assoziation zwischen Tumor Budding und Überleben (OS, CSS, DFS): Signifikant in 8/9, unabhängig in 7/9 Studien

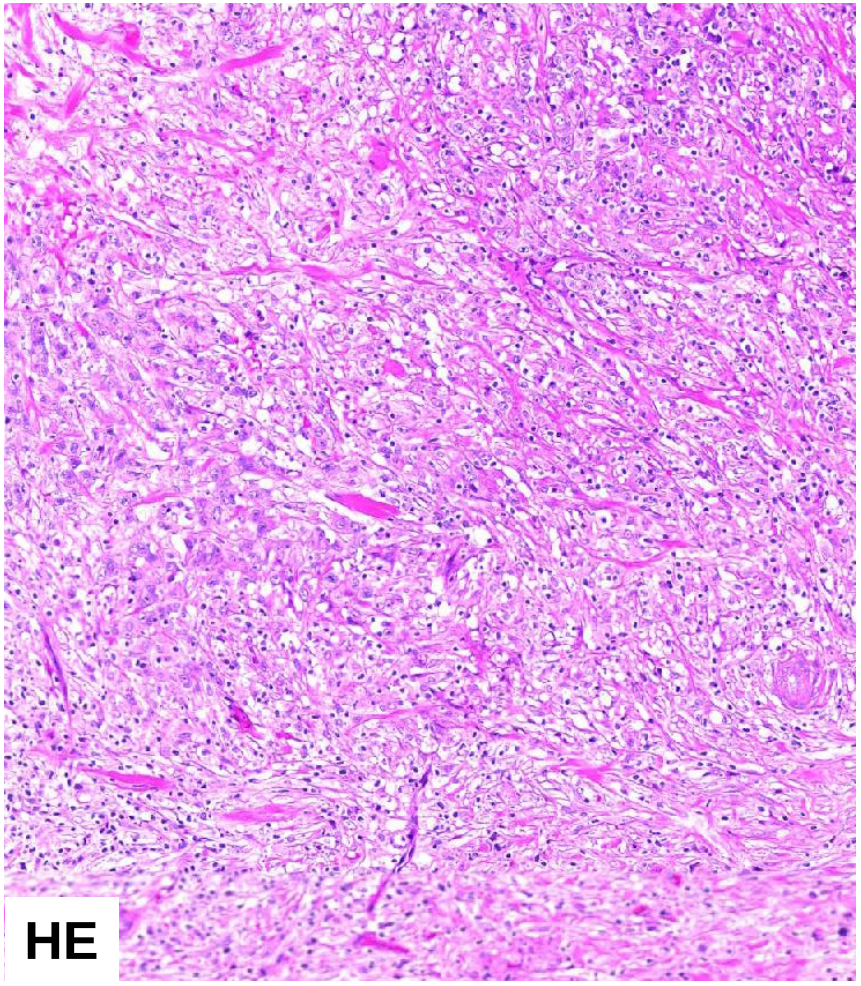
- 1 Meta-Analyse (Petrelli 2015)
  - HG Budding assoziiert mit schlechterem 5-JÜL (OR 6.25, 95%CI 4.04-9.67); p<0.0001)

GRADE-Evidenz: Hoch

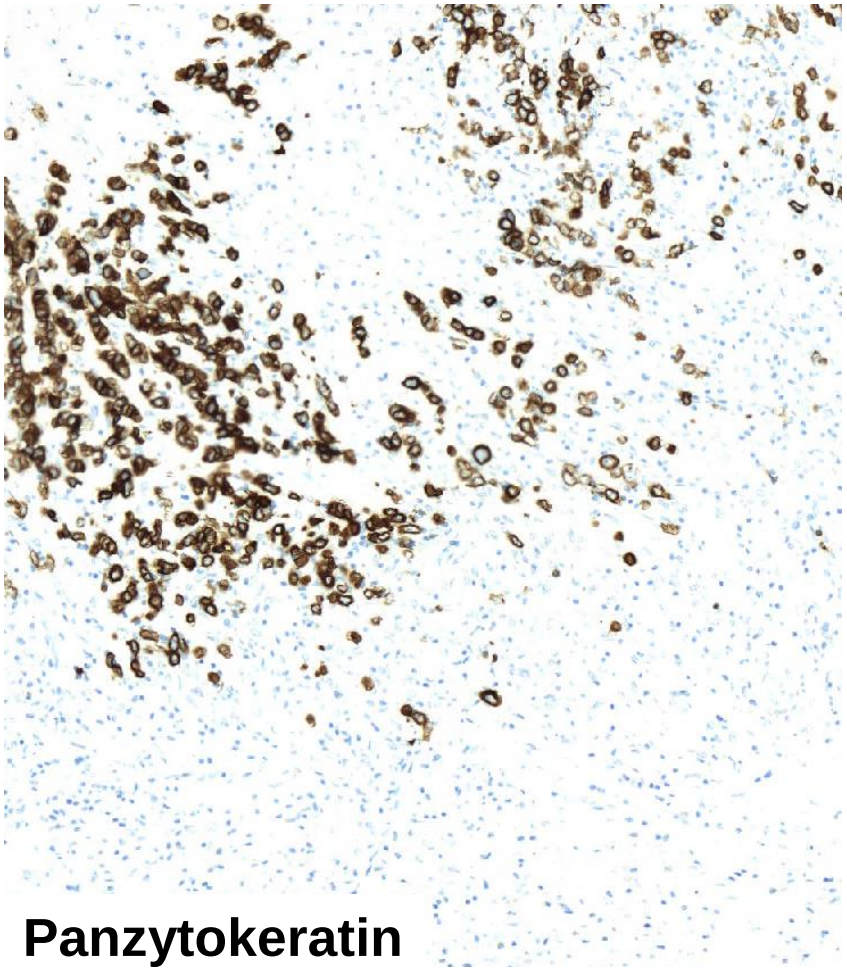
- Prädiktiv: keine publizierten Studien (QUASAR)

Session 3
HE oder IHC?

UNIVERSITÄT BERN



HE



Panzytokeratin

Session 3
HE oder IHC?

UNIVERSITÄT BERN

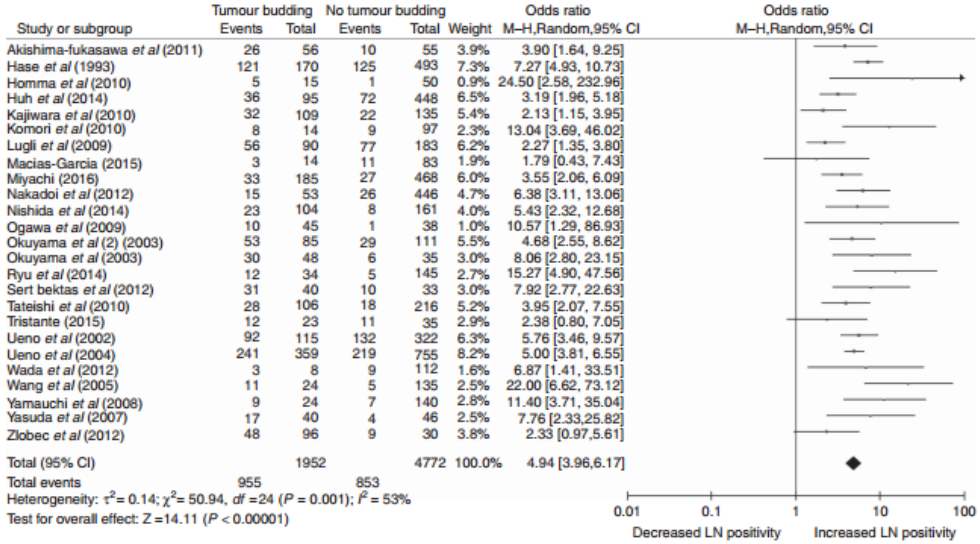


Figure 3. The association of tumour budding with lymph node metastasis in resected colorectal cancer.

Rezidiv: OR 5.73

11/12 HE
1/12 IHC

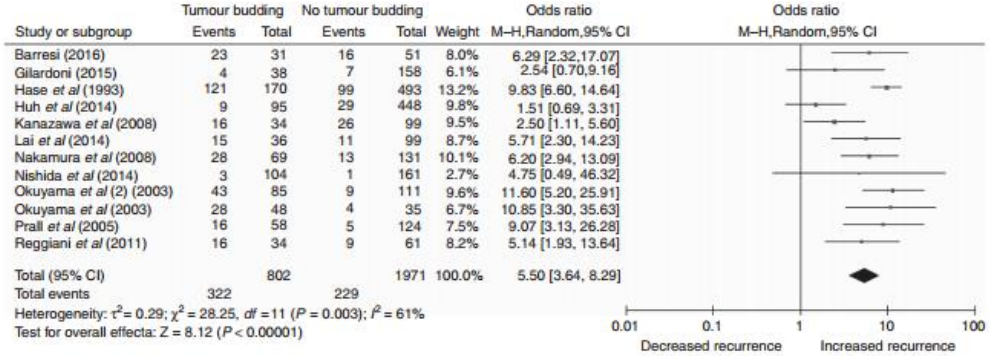


Figure 4. The association of tumour budding with local or distal recurrence in resected colorectal cancer.

5-JÜL: OR 4.51

8/9 HE
1/9 IHC

Kieran Sheahan, Irland; Rogers et al, Br J Cancer 2016

Session 3
HE oder IHC?

UNIVERSITÄT BERN

Pathology International

Pathology International 2016 doi:10.1111/pin.12374

Original Article

Cytokeratin immunohistochemistry improves interobserver variability between unskilled pathologists in the evaluation of tumor budding in T1 colorectal cancer

Keita Kai,[1] Shinichi Aishima,[1,2] Shigehisa Aoki,[2] Yukari Takase,[2] Kazuyoshi Uchihashi,[2] Masanori Masuda,[2] Aki Nishijima-Matsunobu,[2] Mihoko Yamamoto,[1,2] Kousuke Ide,[2] Atsushi Nakayama,[2] Makiko Yamasaki[1,2] and Shuji Toda[2]

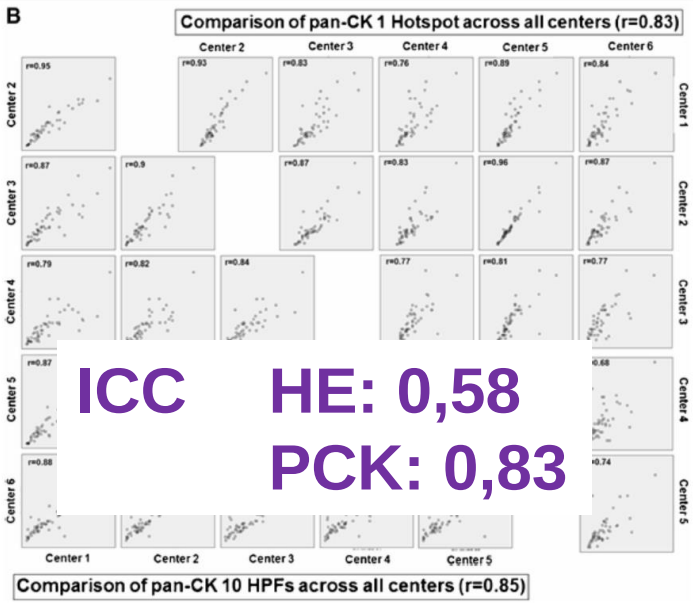
[1]*Department of Pathology, Saga University Hospital and* [2]*Departments of Pathology & Microbiology, Faculty of Medicine, Saga University, Saga, Japan*

Virchows Arch (2015) 466:485–493
DOI 10.1007/s00428-015-1740-9

ORIGINAL ARTICLE

Tumor budding in colorectal cancer revisited: results of a multicenter interobserver study

Viktor H. Koelzer · Inti Zlobec · Martin D. Berger · Gieri Cathomas · Heather Dawson · Klaus Dirschmid · Marion Hädrich · Daniel Inderbitzin · Felix Offner · Giacomo Puppa · Walter Seelentag · Beat Schnüriger · Luigi Tornillo · Alessandro Lugli



ICC HE: 0,58
PCK: 0,83

Die meisten Daten basieren auf HE
IHC könnte zu besserer IOV führen
3-4x mehr Buds werden mit IHC gesehen

Session 4

Intratumorales Budding in Biopsien

UNIVERSITÄT BERN

Relevanz: Entscheidungshilfe neoadjuvante Therapie

- 6 retrospektive Kohortenstudien (zusammen 743 Patienten),

    - Heterogen bezüglich Endpunkte
    - 1 Studie mit neoadjuvanter Therapie
    - RR für Lymphknotenmetastasen 3.0 (95% CI 2.0-4.5)

- Probleme: Fragmente mit invasivem Karzinom, Artefakte usw.

GRADE-Evidenz: Gering

Session 6

Kategorien oder kontinuierliche Werte?

UNIVERSITÄT BERN

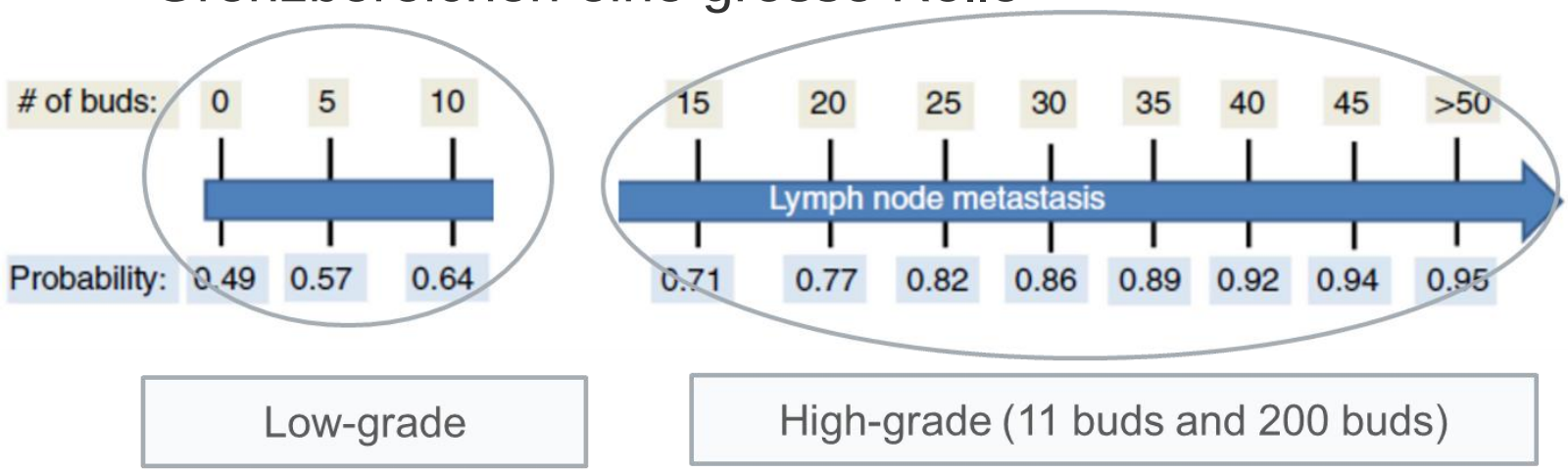
Vorteil Kategorisierung:

Einfacher für klinische Entscheidungen

Nachteil Kategorisierung:

Starke Minderung der statistischen Aussagekraft

Inter- und Intra-Observervariabilität spielt in Grenzbereichen eine grosse Rolle



Conference Proceedings

Consensus statements

UNIVERSITÄT BERN

MODERN PATHOLOGY (2017), 1–13

Recommendations for reporting tumor budding in colorectal cancer based on the International Tumor Budding Consensus Conference (ITBCC) 2016

Alessandro Lugli[1,22], Richard Kirsch[2,22], Yoichi Ajioka[3], Fred Bosman[4], Gieri Cathomas[5], Heather Dawson[1], Hala El Zimaity[6], Jean-François Fléjou[7], Tine Plato Hansen[8], Arndt Hartmann[9], Sanjay Kakar[10], Cord Langner[11], Iris Nagtegaal[12], Giacomo Puppa[13], Robert Riddell[2], Ari Ristimäki[14], Kieran Sheahan[15], Thomas Smyrk[16], Kenichi Sugihara[17], Benoît Terris[18], Hideki Ueno[19], Michael Vieth[20], Inti Zlobec[1] and Phil Quirke[21]

[1]Institute of Pathology, University of Bern, Bern, Switzerland; [2]Pathology and Laboratory Medicine, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, Canada; [3]Division of Molecular and Diagnostic Pathology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; [4]University Institute of Pathology, Lausanne University Medical Center, Lausanne, Switzerland; [5]Institute of Pathology, Kantonsspital Liestal, Liestal, Switzerland; [6]Dynacare Laboratory, Brampton, Ontario, Canada; [7]Pathology Department, Saint-Antoine Hospital, Pierre et Marie Curie University, Paris, France; [8]Department of Pathology, Copenhagen University Hospital, Herlev, Denmark; [9]Department of Pathology, University Hospital Erlangen, Erlangen, Germany; [10]Department of Anatomic Pathology, University of California, San Francisco, CA, USA; [11]Institute of Pathology, Medical University of Graz, Graz, Austria; [12]Department of Pathology, Radboud University Medical Centre, Nijmegen, The Netherlands; [13]Department of Clinical Pathology, Geneva University Hospital, Geneva, Switzerland; [14]Department of Pathology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; [15]Department of Pathology, St Vincent's University Hospital, Dublin, Ireland; [16]Divisions of Anatomic Pathology and Mayo Clinic, Rochester, MN, USA; [17]Department of Surgical Oncology, Tokyo Medical and Dental University, Graduate School of Medical and Dental Sciences, Bunkyo-ku, Tokyo, Japan; [18]Pathology Department, Hôpital Cochin and Université Paris Descartes Sorbonne Paris Cité, Paris, France; [19]Department of Surgery, National Defense Medical College, Tokorozawa, Saitama, Japan; [20]Institute of Pathology, Klinikum Bayreuth, Bayreuth, Germany and [21]Pathology and Tumour Biology, University of Leeds, St James's University Hospital, Leeds, UK

Mod Pathol. 2017 May 26. doi: 10.1038/modpathol.2017.46

Conference Proceedings

Consensus Statements

UNIVERSITÄT BERN

Ein Tumor Bud ist eine Tumoreinzelzelle oder eine kleine Gruppe von Tumorzellen (4 oder weniger)

22/22 (100%), Empfehlung: Hoch, Evidenz: Hoch

Tumor Budding wird am HE ausgezählt.

19/22 (86.4%), Empfehlung: Hoch, Evidenz: Moderat

Tumor Budding wird in einem Hotspot (0.785 mm^2) an der invasiven Tumorfront ausgezählt.

22/22 (100%), Empfehlung: Hoch, Evidenz: Moderat

Intratumorales Budding existiert und ist assoziiert mit Lymphknotenmetastasen.

22/22 (100%), Empfehlung: Hoch, Evidenz: Niedrig

Ein dreistufiges System sollte zusammen mit der Anzahl Buds rapportiert werden, um die Risikoeinschätzung zu vereinfachen.

23/23 (100%), Empfehlung: Hoch, Evidenz: Moderat

Lugli et al, Mod Pathol 2017

Conference Proceedings

Consensus Statements

UNIVERSITÄT BERN

Tumor Budding ist ein unabhängiger Risikofaktor für Lymphknotenmetastasen beim pT1 kolorektalen Karzinom.

23/23 (100%), Empfehlung: Hoch, Evidenz: Hoch

Tumor Budding ist ein unabhängiger ungünstiger Prognosefaktor beim Stadium II kolorektalen Karzinom.

23/23 (100%), Empfehlung: Hoch, Evidenz: Hoch

Tumor Budding soll mit anderweitigen klinisch-pathologischen Merkmalen an multidisziplinären Besprechungen berücksichtigt werden.

23/23 (100%), Empfehlung: Hoch, Evidenz: Hoch

Tumor Budding und Tumor Grading sind nicht gleich.

23/23 (100%), Empfehlung: Hoch, Evidenz: Hoch

Tumor Budding sollte in Richtlinien und Protokolle für die Rapportierung kolorektaler Karzinome einbezogen werden.

23/23 (100%), Empfehlung: Hoch, Evidenz: Hoch

Lugli et al, Mod Pathol 2017

…und so soll’s gehen:

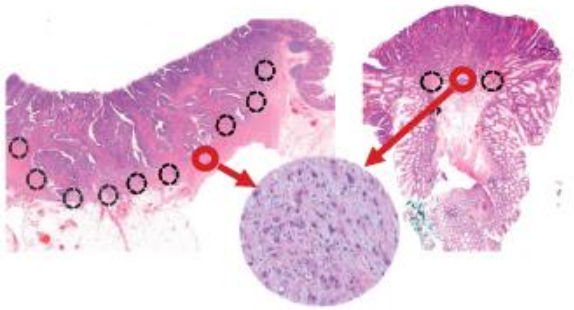
UNIVERSITÄT BERN

1) Konversionstabelle beachten
→ Was ist mein Normalisationsfaktor?

Objective magnification: 20		
Eyepiece FN Diameter (mm)	Specimen Area (mm2)	Normalization Factor
18	0.636	0.810
19	0.709	0.903
20	0.785	1.000
21	0.866	1.103
22	0.950	1.210
23	1.039	1.323
24	1.131	1.440
25	1.227	1.563
26	1.327	1.690

2) Geeigneten Schnitt auswählen

3) Buds bei 20x auszählen und durch Normalisationsfaktor teilen → **0.785 mm²**



Lugli et al, Mod Pathol 2017

Tumor Budding
Besondere Situationen

UNIVERSITÄT BERN

1) Muzinöses und siegelringzelliges Karzinom: Datenlage limitiert/inexistent

- → Tumor Budding nur in Arealen glandulärer Formationen
- → Falls nicht vorhanden: Tumor Budding ‘nicht anwendbar’

2) Peritumorale Entzündung erschwert Erkennen von Tumor Buds

- → PCK zur Orientierung erlaubt
- → Auszählen am HE

3) Z. n. neoadjuvanter Therapie: Datenlage limitiert

- → Tumor Budding ‘nicht anwendbar’

Tumor Budding berichten

UNIVERSITÄT BERN

Budding 1 (x buds / hotspot, 0.785mm²; low)

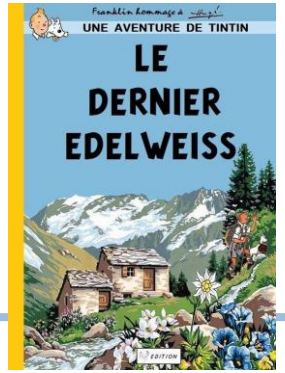
Budding 2 (x buds / hotspot, 0.785mm²; intermediate)

Budding 3 (x buds / hotspot, 0.785mm²; high)

Risikofaktor für pT1

Low: 0-4 buds
Intermediate: 5-9 buds
High: ≥10 buds ⟸ Risikofaktor für Stadium II

Vorgeschlagene Abkürzung: Bd1, Bd2, Bd3



Lugli et al, Mod Pathol 2017

Übersicht

UNIVERSITÄT BERN

Hintergrund

Tumor Budding: Biologie und Anwendungsmöglichkeiten

ITBCC 2016

Zusammenfassung

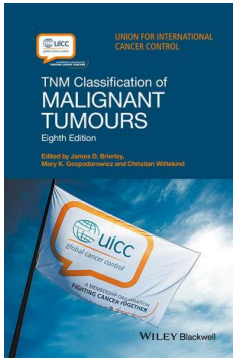
ITBCC
Wie geht es weiter?

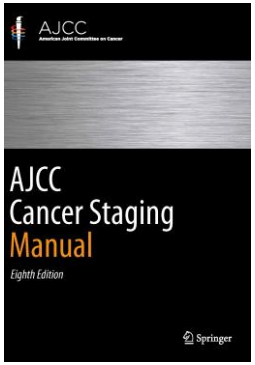
UNIVERSITÄT BERN

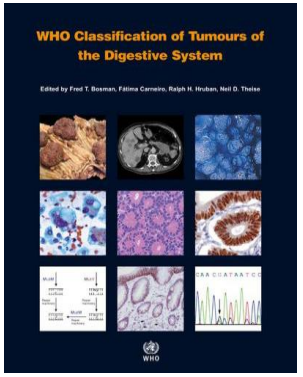
ITBCC 2016 Conference proceedings

CAP, AJCC, ESP, SGPath/ÖGP, ASCO GI

Richtlinien und Protokolle







Wie geht es weiter?
Ongoing studies

UNIVERSITÄT BERN

ITBWG:

Stadium II Studien

HE vs PCK in grossen Kohorten ← **QUASAR**

pT1 CRC

HE vs PCK
Umfassende Analyse von RF ← **Multizentrische Studie**

Prä-operative Biopsien

Prädiktiver Wert Tumorregression ← **Prospektive Studie UniBE**

Digitale Pathologie

HE vs PCK ← **Unterschiedliche Szenarien**

Acknowledgements

Die Teilnehmer der ITBCC

UNIVERSITÄT BERN

ITBCC Bern Switzerland April 27-29 2016

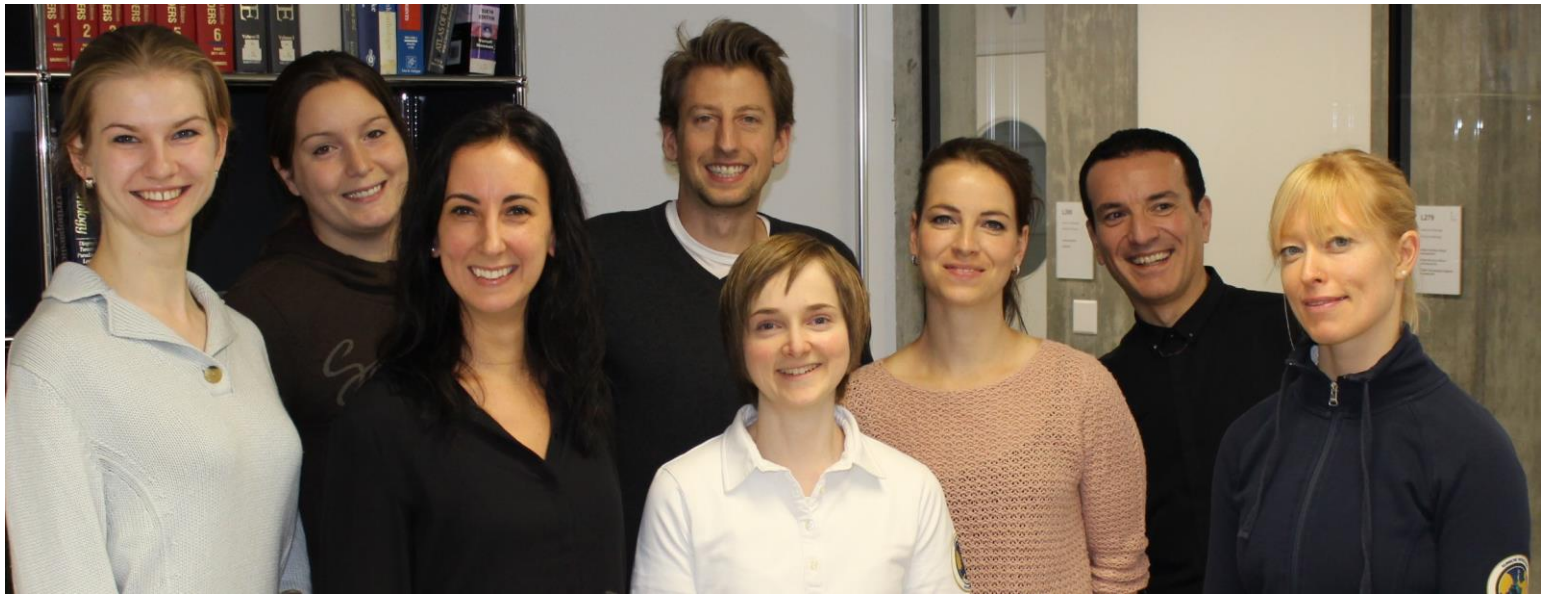
F Bosman TP Hansen P Quirke B Terris J-F Fléjou M Vieth R Riddell A Ristimäki C Langner T Smyrk K Sheahan

S Kakar Y Ajioka G Puppa K Sugihara R Kirsch I Zlobec A Lugli H El-Zimaity I Nagtegaal G Cathomas S Brockmoeller H Dawson H Ueno

ACKNOWLEDGMENTS

Interdisciplinary CRC Research Group, Institute of Pathology, University of Bern, Switzerland:

Prof. Dr. med. Alessandro Lugli
Prof. Inti Zlobec
Dr. med. A. Blank
Lena Sokol
Stephan Zahnd
Kris Uth
M Med Monique Niklaus

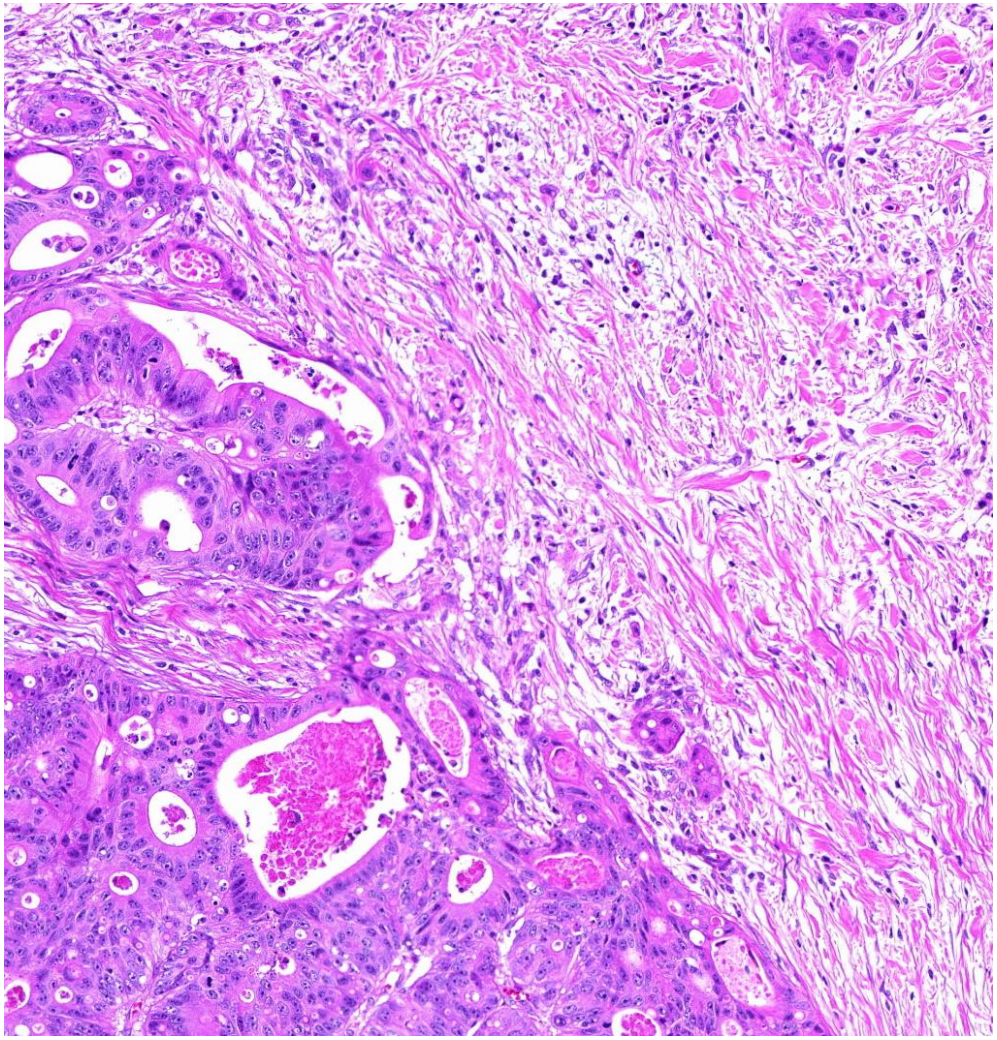


Danke für Ihre Aufmerksamkeit!

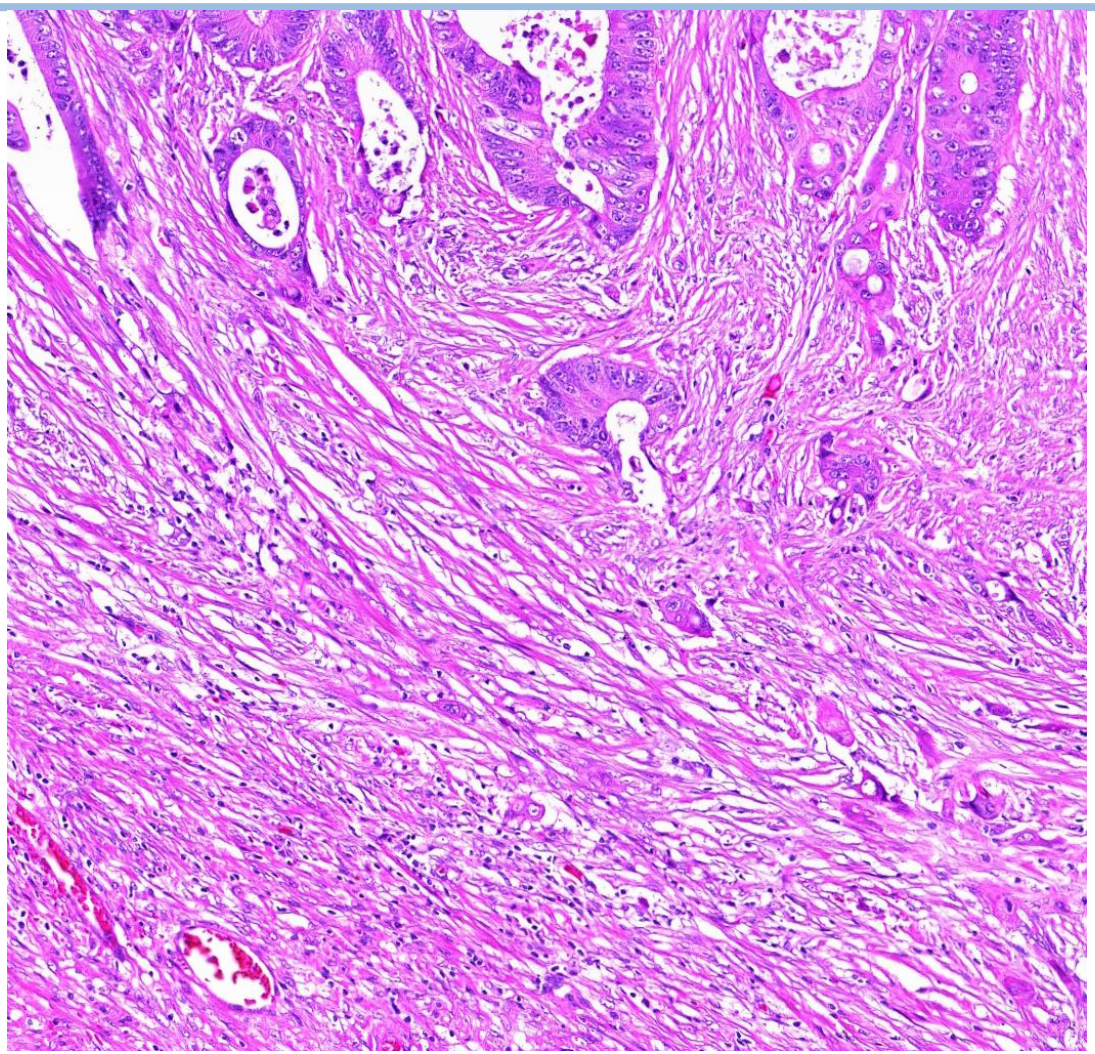
UNIVERSITÄT BERN

Bd1
0-4 Buds

UNIVERSITÄT BERN



Bd2
5-9 Buds



Bd3

10 Buds oder mehr