



MINISTRY OF PUBLIC HEALTH

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NATIONAL CANCER TREATMENT GUIDELINES

Issue 1 - October 2012

NATIONAL CANCER TREATMENT GUIDELINES





Scientific Committee

List of drug distribution centers

Scientific Committee for the review of cancer treatment request forms

Name	specialization
Dr. Walid Ammar	Director general of the Ministry of Health and head of the scientific committee
Dr. Fadia Elias	Oncology specialist
Dr. Hassan Khalifeh	Hematology and pediatric oncology specialist
Dr. Ali Taher	Hematologist and oncology specialist
Dr. Wagih Saad	Oncology specialist

List of drug distribution centers in all regions

Central drug distribution center at Karantina
Drug distribution center in Saida Governmental Hospital
Drug distribution center in Nabatieh Governmental Hospital
Drug distribution center in Tripoli Governmental Hospital
Drug distribution center in President Elias ElHraoui Governmental Hospital in Zahle
Drug distribution center in Beiteddine Medical Center

اللجنة العلمية لدراسة طلبات أدوية السرطان

الصفة	الإسم
مدير عام وزارة الصحة العامة ورئيس اللجنة العلمية	الدكتور وليد عمار
أخصائي أمراض سرطانية	الدكتورة فاديا الياس
أخصائي أمراض الدم والأورام عند الأطفال	الدكتور حسن خليفة
أخصائي بأمراض الدم والتورم الخبيث	الدكتور علي طاهر
أخصائي أمراض سرطانية	الدكتور وجيه سعد

لائحة بمراكز توزيع الأدوية في جميع المناطق اللبنانية

المركز الرئيسي لتوزيع الأدوية في الكرنيتينا
مركز توزيع الأدوية في مستشفى صيدا الحكومي
مركز توزيع الأدوية في مستشفى النبطية الحكومي
مركز توزيع الأدوية في مستشفى طرابلس الحكومي
مركز توزيع الأدوية في مستشفى الرئيس الياس الهراوي الحكومي زحلة
مركز توزيع الأدوية في مركز بيت الدين الصحي





Antineoplastic Drugs/NCR

Patient Information

رقم الهوية: _____ رقم بطاقة الكرتينا: _____
إسم المريض: _____ إسم الأب: _____ الشهرة: _____
إسم الأم: _____ تاريخ الولادة: --/--/-- الجنس: ذكر أنثى
العنوان
المحافظة: _____ القضاء: _____ البلدة: _____
الشارع: _____ الملك: _____ هاتف: --/-----

Tumor Registry Information

Height: _____ cm Weight: _____ kg BSA: _____ m²
ICD-10 Specific Diagnosis: _____
Primary Site (Text): _____
Laterality: Right Left Bilateral Not applicable Unspecified Date of first diagnosis: _____
Pathology: _____ ICD-10 M
Pathology Center: _____ Pathologist: _____
Classification: TNM⁽²⁾ T N M Stage⁽³⁾: _____ Grade: _____ Other Staging: _____
Protocol: _____ Expected Duration of treatment for new cases: _____
Type of report: New case Known case  Relapse  Loco-Regional
 Progression Distal
 Renewal ⁽⁴⁾

Treatment

Finality of treatment: Palliative only Other
Prior treatment: No Yes⁽⁴⁾ Specify: _____
Type of treatment planned:
Surgery: No Yes _____
Chemotherapy⁽⁵⁾: No Yes _____
Radiotherapy: No Yes _____
Targeted therapy: No Yes _____
Immunotherapy: No Yes _____
Hormone therapy: No Yes _____

Physician Information

Physician Name: _____ LOP Registration No.: _____

Specialty: _____ Telephone:/.....

Date:...../...../.....

Signature & Stamp: _____

Documents to be submitted:

- 1 صورة الهوية أو إخراج القيد
- 2 NCR
- 3 Oncology report تقرير الطبيب
- 4 Pathology نتيجة الزرع
- 5 صورة عن تقارير الصور الشعاعية
- 6 Oncology prescription with exact dosage & duration
please write clearly الوصفة الطبية
- 7 copy of drug dispensing center patient card should be submitted
(if available) (صورة عن بطاقة مرآز توزيع الأدوية (إذا وجدت)

N.B:

- 1 This form must be completed by the doctor.
- 2 All information should be attached.
- 3 All attached reports and studies should be original and official.

- (1) For reporting to NCR: send form to Epidemiological Surveillance Unit Program by postal mail Ministry of Public Health Museum. Beirut or by fax 01-610920
- (2) TNM classification is based on pathology results.
- (3) Documented evidence should be submitted for Stage IV.
- (4) Copy of Drugs Dispensing Center Patient Card should be submitted (if applicable).
- (5) If neoadjuvant chemotherapy, please specify date of treatment.



Preface

Upon the request of the Minister of Health, the **UNDP TOKTEN** project is launching the National Cancer Treatment Guidelines (second edition) based on the latest scientific updates. The first edition of the National Cancer Treatment Guidelines in 2010 had a very positive outcome that resulted in the provision of international standards of care for cancer patients subsidized by the Ministry of Health, Similarly to the first edition, an official national committee including 7 prominent Lebanese oncologists from different backgrounds resumed work on the guidelines supported by the **TOKTEN** project manager *Mrs. Ariane Elmas Saikali*. The outputs of the committee were transmitted to Lebanese expatriate oncologists from distinguished international cancer centers to be reviewed, discussed and approved. We are thankful to a Lebanese Expatriate, *Mr. Monzer Hourani*, who funded the publication of this booklet

Acknowledgments

We are honored to have cooperated with *Minister Ali Hassan Khalil* and his distinguished team who have demonstrated a persistent commitment to provide international standards of care for cancer patients.

I would like to take this opportunity to thank all the persons who contributed to the successful completion of the guidelines and enabled the proper accomplishment of this initiative. I am extremely grateful to the distinguished oncologists of the national and international committees who volunteered their time, profound knowledge and extensive expertise for the aim of providing the optimal treatment protocols.

I would like to acknowledge the vital participation of each member of the national committee in elaborating evidence based protocols. The guidelines are a direct result of the dedication and perseverance of *Dr. Fadia Elias, Dr. Joseph Kattan, Dr. Ghazi Nsouli, Dr. Ziad Salem, Dr. Ali Shamseddine and Dr. Ali Taher*. Special recognition is extended to the head of the committee *Dr. Nizar Bitar* for his valuable leadership and guidance. This project could not have been accomplished without the valuable contribution of our reviewers from international cancer centers, namely *Dr. Ahmad Awada, Dr. Fadlo Houry, Dr. Anthony El-Khoueiry, Dr. Nizar Tannir, and Dr. Anas Younnes*. Accordingly, we wish to express our sincere gratitude to the coordinator of the international committee and reviewer *Dr. Jean Pierre Issa* for his relentless support.

I place on record, my sincere gratitude to the advisory support provided to the national committee by outstanding oncologists in particular *Dr. Muheiddine Seoud, Dr. Fadi Geara, Dr. Arafat Tfayli, Dr. Mohamed Kharfan-Dabaja and Dr. Hassan Khalifeh*.

I also would like to thank other oncologist who provided their inputs namely *Dr. Fadi El Karak, Dr. Fadi Farhat and Dr. Samar Muwakkit*.

It is a pleasure to also thank *Mr. Monzer Hourani* for his financial support and constant encouragement for the completion of this project.

Lastly, I would like to acknowledge and commend all contributors for their efforts, cooperation and collaboration towards the success of this project.

Robert Watkins
UNDP Resident Representative

مقدمة الإصدار الثاني لبروتوكولات علاج الأمراض السرطانية

بمناسبة الإصدار الثاني للبروتوكولات العلاجية للأمراض السرطانية نود أن نؤكد على جملة أمور نعتمدها كأساس لسياستنا الصحية في مجالات الأمراض السرطانية:

أولاً إن الأمراض السرطانية رغم صعوبتها فإن التطورات الحاصلة على صعيد التشخيص والاكتشافات الدوائية تجعل من الممكن مواكبة المرض والسيطرة عليه في كثير من الأحيان، وتبقى أساليب العلاج وتأمين متطلباته وتغطية كلفته هو التحدي الأساس.

وفي لبنان تم تسجيل في العام 2010 (السجل الإحصائي لوزارة الصحة العامة) 8400 حالة سرطان جديدة، و25000 حالة استشفاء وكلفت 53% من كلفة أدوية الأمراض المستعصية التي تغطيها الوزارة.

ثانياً إن وزارة الصحة العامة ستبقى تبذل الجهود المطلوبة لتأمين الأدوية الخاصة بالأمراض السرطانية التي تقدمها مجاناً للمرضى المعالجين على نفقة الوزارة وهم يقاربون 51% من الشعب اللبناني.

وهي تقوم بتوزيع هذه الأدوية عبر المستودع المركزي في الكرتينا، إضافة لخمسة مراكز توزيع تم إنشاؤها وتجهيزها في المناطق: في مستشفيات طرابلس لبقية في الشمال، وزحلة المعلقة في البقاع، وصيدا الحكومي في الجنوب، ومستشفى النبطية، وبيت الدين الحكومي في جبل لبنان. ويشرف على كل مركز توزيع صيدلي مختص. وهذه المراكز مرتبطة إلكترونياً بالمستودع المركزي لمنع الازدواجية والهدر.

ثالثاً متابعة اعتماد اللجنة الفنية الخاصة بالأمراض السرطانية المرجع العلمي الوحيد المكلف دراسة ملفات المرضى المقدمة لوزارة الصحة بهدف الحصول على المساعدة بالأدوية. ولها الحق في تقرير ما تراه مناسباً أو قبول الطلب أم رفضه أم طلب فحوصات إضافية أو سواها، ولقد توزعت مهام اللجان حديثاً بشكل يساعد على تسهيل المعاملة والبت بها وفق الاختصاصات المتفرعة عن المرض.

رابعاً اعتماد البروتوكولات الطبية الموضوعية والمعتمدة من قبل الوزارة والتي ساهم في وضعها نخبة كبيرة من كبار الأخصائيين اللبنانيين ومن الخارج والتي اعتمدت المعايير الدولية المعتمدة عالمياً.

ولجنة البروتوكولات العلمية تأخذ بالاعتبار كل المستجدات الحاصلة في مجالات التشخيص والعلاج والمتابعة والكلفة.

ولقد أكدت كل الدراسات العالمية عدم وجود أي ارتباط بين كلفة الدواء والنتيجة المحصلة، وهذا يعني أن الأدوية الباهظة الثمن ليست بالضرورة الأفضل لمعالجة السرطان.

وهنا نؤكد على أهمية العمل مع نقابتي الأطباء والجمعيات العلمية المعنية بالأمراض السرطانية على ترشيد الوصفة الطبية والبروتوكولات الطبية المعتمدة تشكل الأساس لترشيد الوصفة الطبية.

خامساً إن توفر العلاجات المناسبة والبروتوكولات الطبية لا تقلل من أهمية العمل في مجالات الوقاية من

الأمراض السرطانية حيث تأكدت العلاقات المباشرة مع الأنماط الغذائية السيئة والتدخين والتلوث وسواها. كما تأكدت أهمية برامج الاكتشاف المبكر كما سبق وذكرنا. إننا في النهاية وبمناسبة الإصدار الجديد لبروتوكولات علاج السرطان والذي كان نتيجة لمراجعات ودراسات ومناقشات وملاحظات كل الجمعيات العلمية المعنية لتوضع بتصرف الجسم الطبي ولتساعد بتحديد العلاجات ضمن أفضل المواصفات العلمية المعتمدة في لبنان والعالم.

ومن الطبيعي أن تتم مراجعة هذا الكتيب بشكل دوري وكلما دعت الحاجة.

إننا نتقدم بالشكر الجزيل والتقدير لفريق العمل من الأطباء والمساعدين الذين ساهموا في وضع هذه البروتوكولات العلمية، وتقدير خاص إلى CDR وإلى منظمة (UNDP) ومشروع Tokten.

وزير الصحة العامة
علي حسن خليل





Introductory Notes

The first edition of the National Cancer Treatment Guidelines represented a milestone for Medical Oncology in Lebanon. By agreeing on a fixed set of detailed protocols, the National Committee for Cancer Treatment ensured that patients with cancer would receive state of the art treatment in Lebanon and at the same time avoid unnecessary and costly treatments that can add to the burden of cancer without providing tangible benefits in terms of survival or even symptom relief. These guidelines were applied in a remarkably rapid and efficient manner as a direct result of the efforts of a group of people including the National Committee, its Chair Dr. Nizar Bitar, and the dedicated physicians at the Ministry of Health. Thanks in part to those efforts, oncology care in Lebanon has been optimized throughout the country in a record amount of time.

When the first edition of the guidelines was published, it was clear that the process would need to be both transparent and flexible enough to allow for changes brought about by new drugs and new medical information. The processes put in place resulted in this second edition, which has seen a revision of many of the guidelines, along with the development of new guidelines for conditions that were not covered previously. As in the initial efforts, the process involved development or revision of guidelines by members of the Lebanese National Committee for Cancer Treatment, followed by peer review by a team of international oncology experts who provided input and suggestions. The result is this second edition – a document Lebanese oncologists should be proud of.

Many challenges remain of course. As Oncology is moving towards personalized medicine, there is a need to ensure the availability, quality control and standardization of molecular tests to select patients for therapy. The process for testing and introducing new drugs should be reviewed and, at the other end of the spectrum, palliative care and adequate pain control need to be optimized in Lebanon. The country's physicians and

Public Health experts should also consider whether enough attention is paid to cancer prevention measures. Hopefully, there will be national efforts to address these issues in the same way efficient way that led to the current guidelines.

On behalf of the team of external reviewers, I would like to express thanks for allowing us to remain involved in this project. When this project started, there was considerable skepticism over whether a consensus could be reached or whether guidelines could be applied in the management of this deadly and emotionally charged disease. The National Committee showed that it can be done and this should serve as a model for the management of chronic diseases in the country. We congratulate you on transforming cancer care in Lebanon and hope that these revised guidelines will continue to be helpful in achieving optimal cancer care in Lebanon.

Jean-Pierre Issa, MD

American Cancer Society Clinical Research
Professor of Medicine

Fels Institute for Cancer Research and Molecular Biology
Director

Program in Cancer Epigenetics, Fox Chase Cancer Center
Leader

Temple University, Philadelphia, USA



Introductory Notes

لقد تشكلت اللجنة الوطنية لبروتوكولات علاج الأورام الخبيثة بموجب قرار صادر عن وزارة الصحة العامة بتاريخ 21 كانون أول 2009 وذلك بهدف ترشيد استخدام الدواء والموارد المتاحة بما لا يتعارض مع مصلحة المريض وينعكس إيجاباً على كلفة علاجه وذلك من خلال لائحة الأدوية المعتمدة في وزارة الصحة العامة.

لقد أنجز هذا العمل بالتنسيق مع السيدة أريان ألماس المديرية المسؤولة عن مشروع توكتن التابع لبرنامج الأمم المتحدة الإنمائي في لبنان.

Tokten = Transfer of Knowledge Through Expatriate Nationals

والممول من المغترب اللبناني السيد منذر حوراني والذي يهدف الى نقل المعرفة عن طريق الرعايا المغتربين والمتفوقين كل في مجاله.

لقد عقدت اللجنة اجتماعاتها الدورية لمناقشة البروتوكولات العلاجية للأمراض الخبيثة في مختلف مراحلها.

تعتبر هذه البروتوكولات نوع من التوجيهات والإرشادات التي تستند الى أسس علمية قوية ومراجع علمية موثوق بها ومثبتة، يتوافق عليها مجموعة من الخبراء والأخصائيين تساعد الممارسين في اتخاذ القرار وتسلط الضوء على مكامن الغموض والتساؤلات ليصار الى مناقشتها ومعالجتها.

لقد استعنا لإنجاز هذا العمل بالعديد من البروتوكولات المعتمدة في الأوساط العلمية الطبية العالمية المختلفة (FDA, EMEA, NCCN, ...) وبالعديد من الزملاء الأخصائيين في لبنان الذين أبدوا آراءهم بمواضيع مشهود لهم فيها. وخرجنا بالإجماع

بمقترحات رفعناها تبعاً لزملاء مشهود لهم في أميركا وأوروبا وأبدوا مقترحاتهم حتى وصلنا الى ما وصلنا اليه.

لم يكن من السهل الفصل في كثير من الأحيان.

لم يكن من السهل أيضاً إثبات التوازن بين إقرار علاج أو عدمه من ناحية، وبين حاجة المريض أو عدم الحاجة الى علاج معين من ناحية أخرى، خاصة عندما يكون العلاج معتمد أو مقترح من قبل بعض الجمعيات العلمية العالمية بالرغم من انتفاء فعالية مثبتة أو وجود فعالية هامشية.

ان ذلك يسمح لنا بالتريث ويفتح الباب أمام إجراء أبحاث ودراسات علمية تأخذ بالإعتبار خصوصيات المريض والمجتمع.

فالكل يعلم غزارة المستجدات العلمية الطبية وهذه المستجدات هي اليوم بمتناول الجميع حتى المريض وأهله وفهمها ليس بالشيء اليسير مما يضع الجسم الطبي تحت ضغط المطالبة باللجوء اليها. وهنا يبرز دور الطبيب بأخذ الوقت الكافي مع المريض قبل اللجوء الى إعطاء الوصفة الطبية، كما يبرز أيضاً دور هذه البروتوكولات في المساعدة باتخاذ القرار ودور اللجنة الفنية في وزارة الصحة المسؤولة عن آلية التطبيق بعد دراسة ملف المريض لاتخاذ القرار النهائي.

لم يكن من السهل أيضاً تقريب وجهات النظر وما أكثرها في هذا المجال. الكل أظهر حذراً لا متناهياً من الإنتقاص من حق المريض ومن الكيل بمكيالين خاصة بما يخص هذه الشريحة من المرضى الذين لا وجود لديهم أية تغطية صحية.

لقد طلب أعضاء اللجنة أن يكون عملهم حر وقراراتهم مستقلة. إن هذا الأمر تم احترامه وأشار الى أن هذا العمل هو تطوعي صرف ولم نتقاضى أي أجر لقاءه.

إن مرضى السرطان بازياد مضطرد خاصة في البلدان النامية وإننا نشهد جيل جديد من الأدوية مختلف من نواح عديدة خاصة فيما يخص كلفته الباهظة والتي لم تعد بمقدور أي مواطن مهما بلغ دخله حيث غدا ويغدو علاج السرطان مسؤولية الدولة وليس مسؤولية المواطن إذ قد توازي موازنة دوائين أو ثلاثة في العام 2012 موازنة وزارة الصحة كاملة للعام 2000.

من هنا إن وضع بروتوكولات علاجية يصبح ضرورة ملحة لممارسة طب متجانس ومتكافئ خاصة في البلدان الغير منتجة والمحدودة الموارد والتي ينتمي أطباؤها الى ثقافات ومرجعيات طبية مختلفة.

لا يمكن اعتبار هذا العمل شامل ولا حصري.

هذا العمل بحاجة لاستمرارية ولمراجعة دورية انسجاماً مع التطورات المستقبلية وهو حلقة من سلسلة تشمل مما تشمله البرامج التثقيفية والوقائية والكشف المبكر ومساعدة المدخنين على الإقلاع، السجل الوطني والأبحاث ووضع أسس العلاجات الملطفة وعدم الهروب منها باللجوء الى الوصفة الطبية. ونأمل من أصحاب القرار المساعدة لوضع الأسس لمركز وطني للسرطان يعمل الجميع تحت سقفه على غرار ما يحدث في الدول المتقدمة.

الدكتور نزار بيطار

الجامعة اللبنانية - كلية العلوم الطبية
رئيس قسم أمراض الدم والاورام
مستشفى الساحل

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01 Head And Neck



Nasopharynx

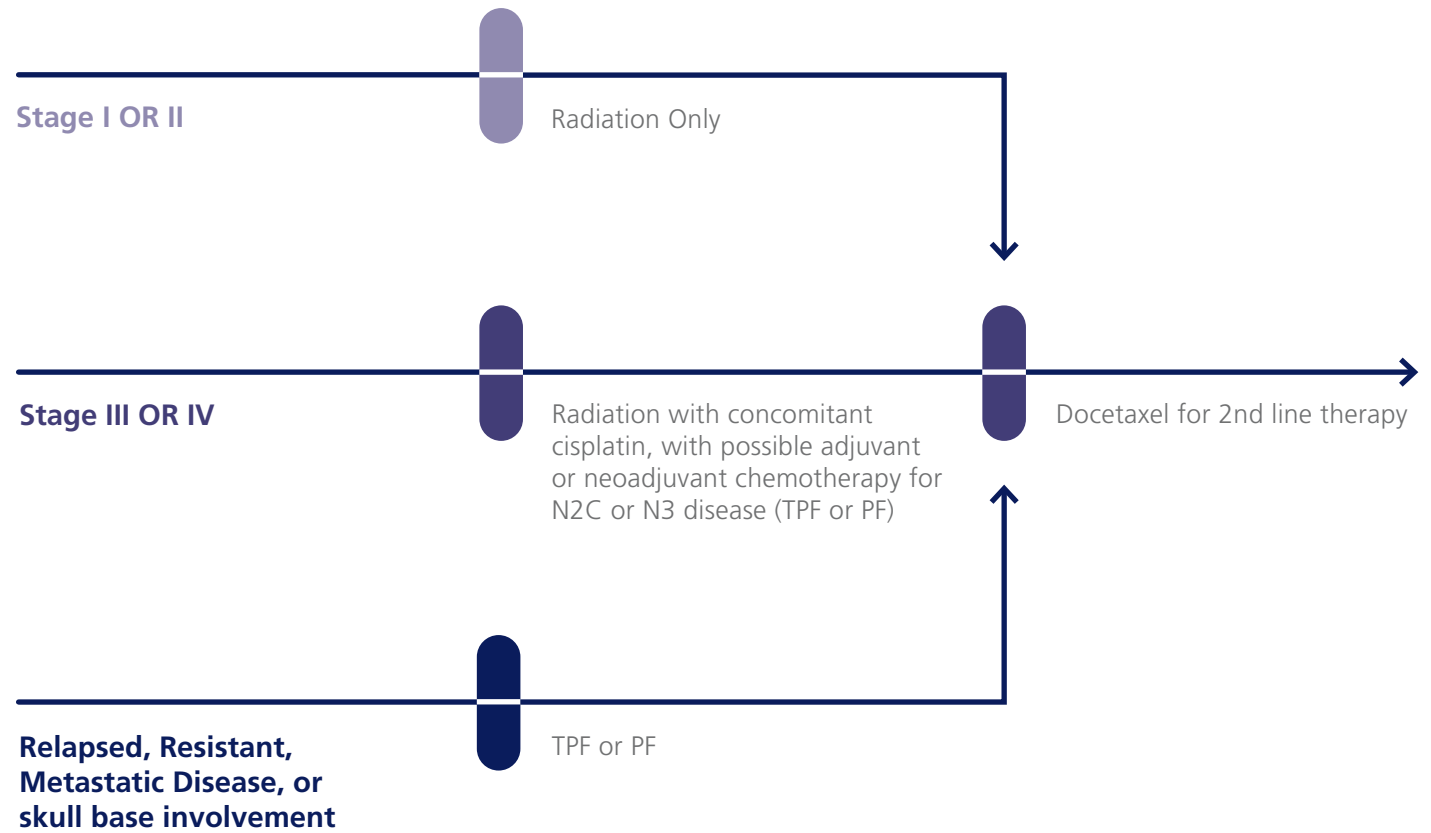
Squamous Cell Cancers
of the Head and Neck

Oropharynx

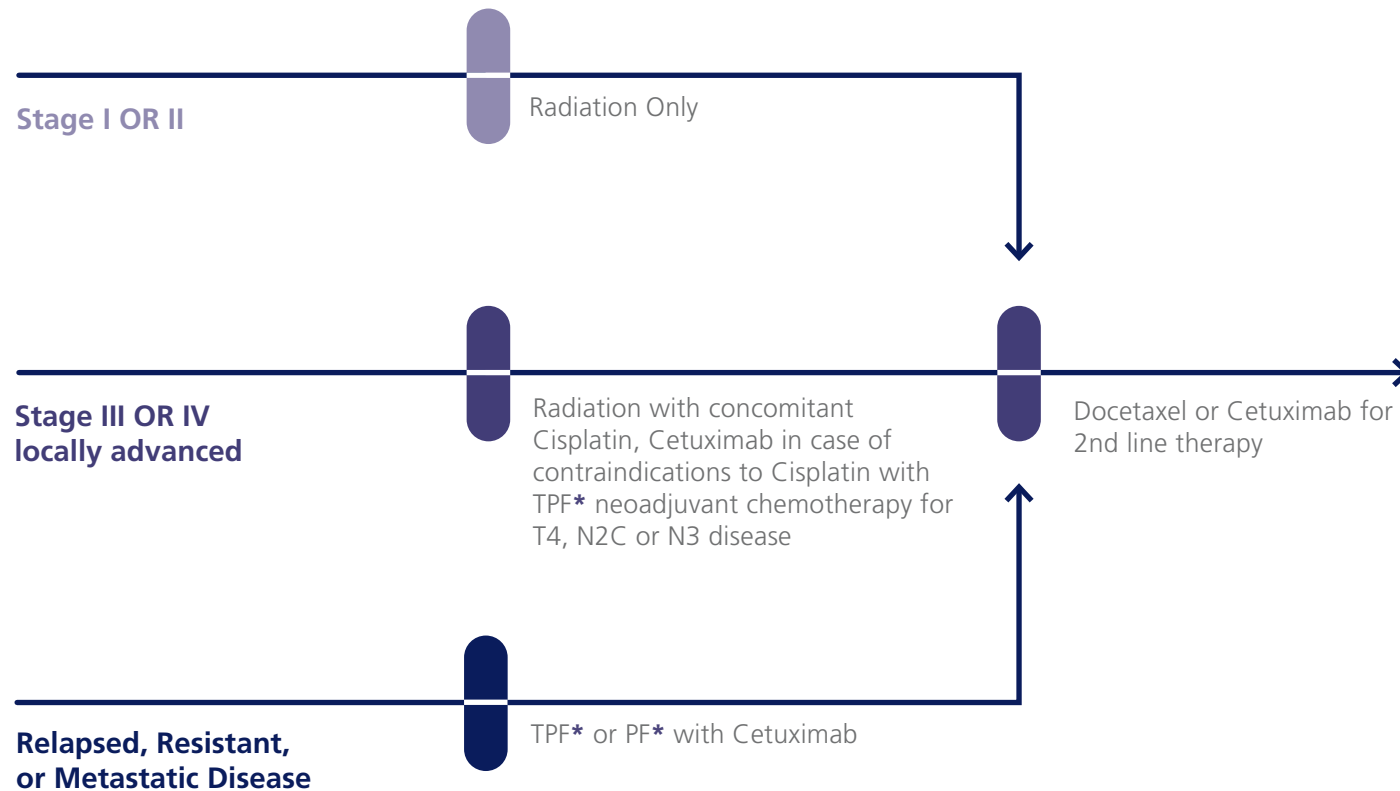
Oral cavity



Nasopharynx



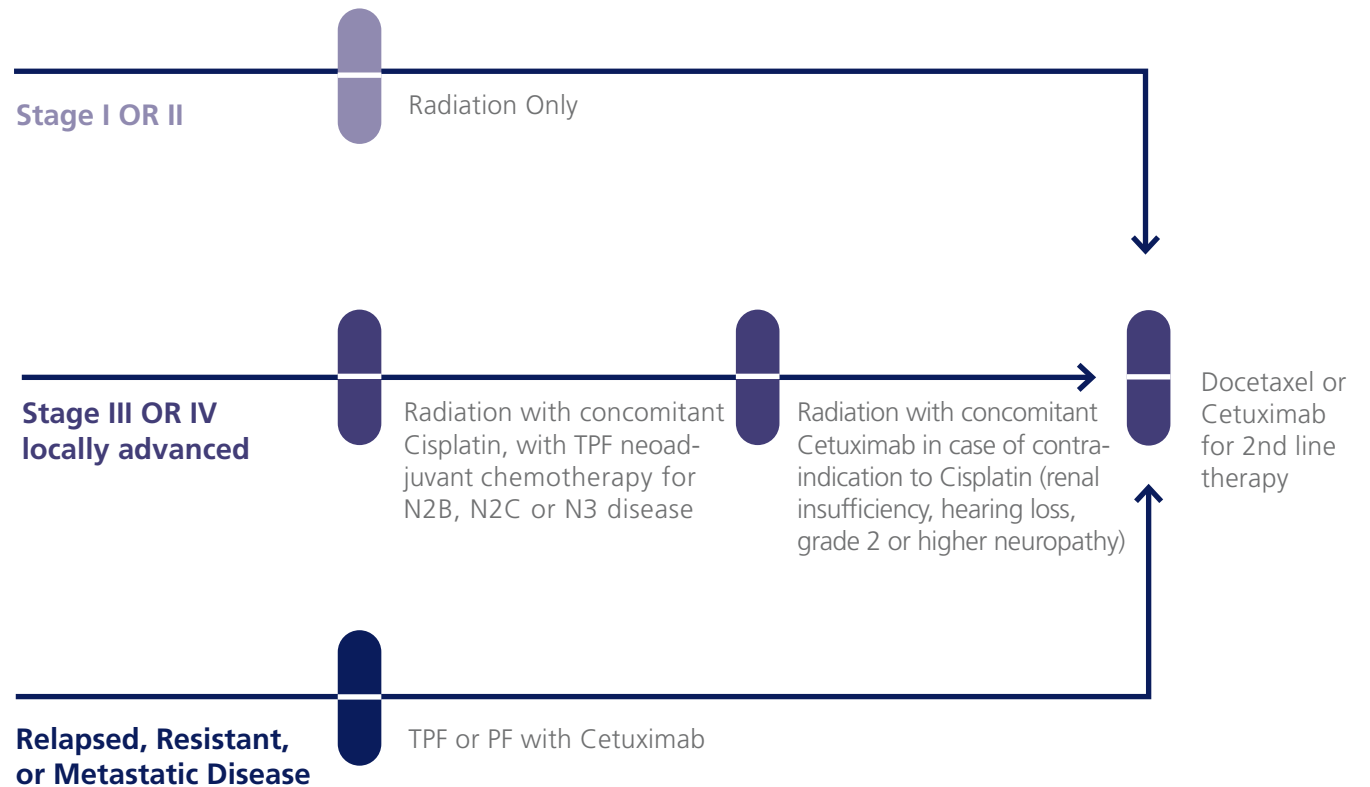
Squamous Cell Cancers of the Head and Neck, Larynx



* TPF: Docetaxel, Cisplatin, 5-FU
PF: Cisplatin, 5-FU

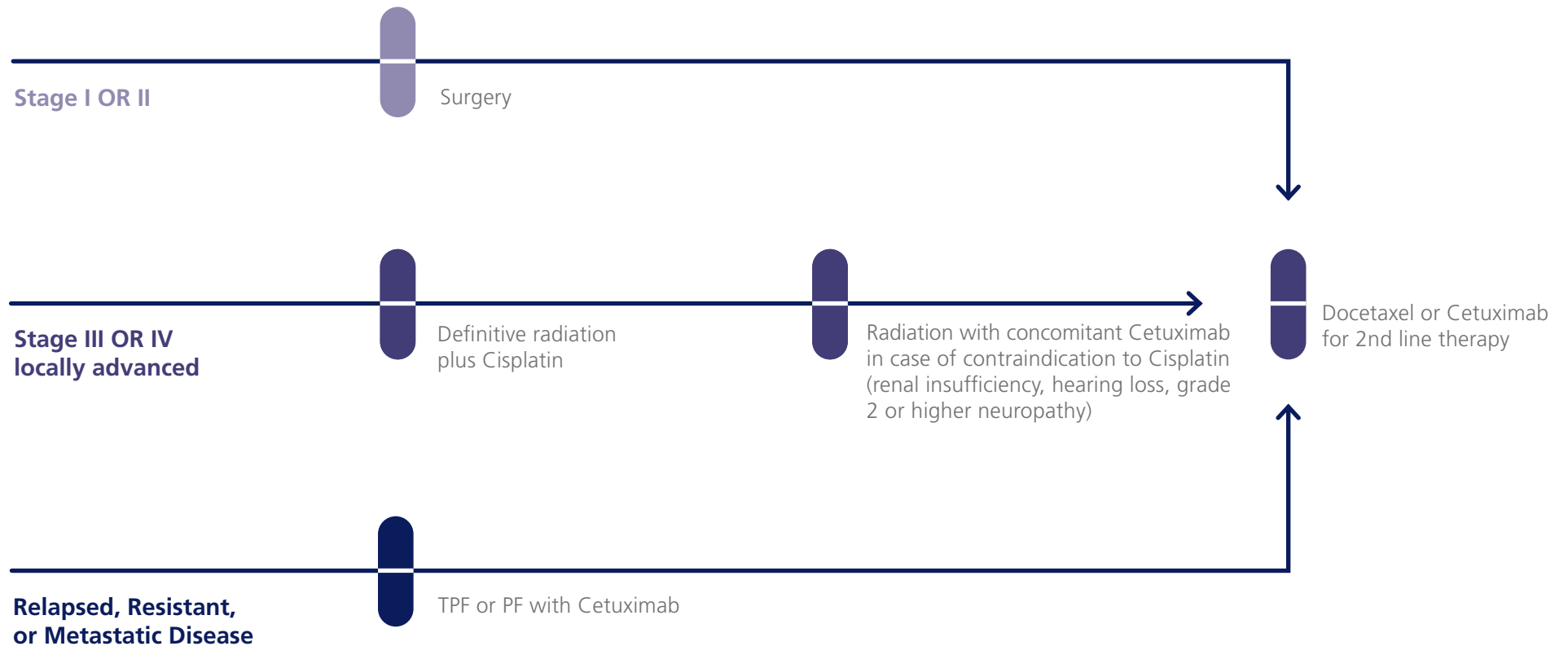


Oropharynx



Consider testing for HPV

Oral Cavity



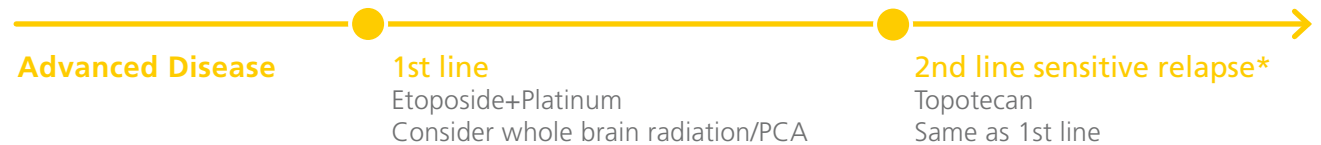
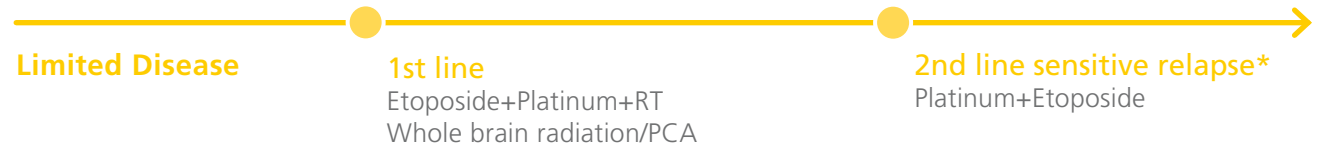
02 Lung Protocols



Small Cell Lung Cancer
Bronchoalveolar Carcinoma
Mesothelioma
Non small cell lung cancer
(except bronchoalveolar)



Small Cell Lung Cancer



*Sensitive relapse: defined as progression no less than 3 months after completion of front-line chemotherapy and preferably 6 months or longer.

Bronchoalveolar Carcinoma



Mesothelioma





Non Small Cell Lung Cancer (Except Bronchoalveolar)

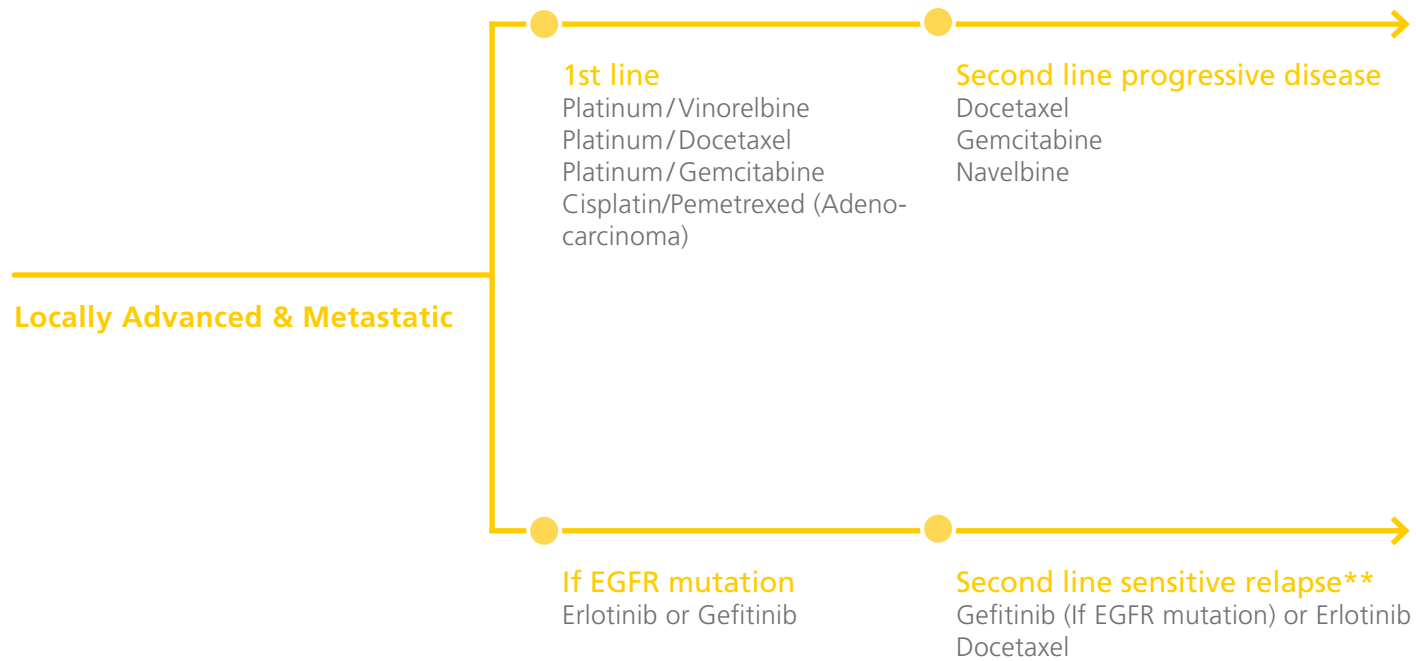
**Adjuvant/Neoadjuvant
for Stages IB to III**

Cisplatin*+Vinorelbine (x4)
Cisplatin+Docetaxel/
Cisplatin+Gemcitabine

Concomitant CT+RT for Stage III

Cisplatin/Vinorelbine
Cisplatin/Etoposide

* Carboplatin if Cisplatin is contraindicated



** Progression 6 months or longer after completion of front-line chemotherapy.
Maximum of 6 cycles of chemotherapy.

03 Breast Cancer



Neoadjuvant

Premenopausal Metastatic Breast Cancer

Postmenopausal Metastatic Breast Cancer

Adjuvant therapy for HER-2/ neu positive tumors

Adjuvant therapy for HER-2/ neu negative tumors

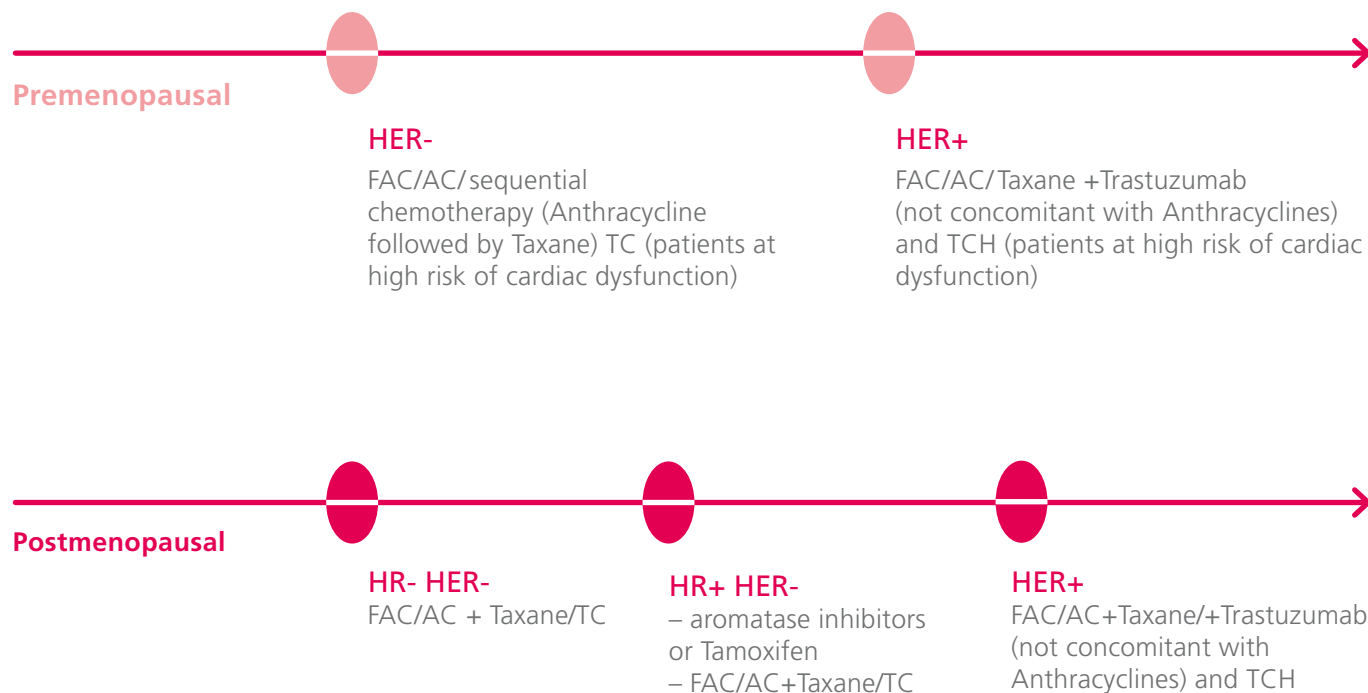
Adjuvant hormone therapy

Adjuvant therapy

Tubular and colloid histology, Node negative



Neoadjuvant



Premenopausal Metastatic Breast Cancer

HR- HER-	HR- HER+	HR+ HER+	HR+ HER-	Non bulky or symptomatic disease	Bulky and/or symptomatic disease
FAC/AC/Taxane/ Taxane Gemcitabine/ Cisplatin Vinorelbine/ Vinorelbine Capecitabine/ Capecitabine/Docetaxel Capecitabine/CMF/ Liposomal Doxorubicin (restricted to decreased EF)	FAC/AC/taxane/ Taxane Gemcitabine/ Cisplatin Vinorelbine/ Vinorelbine Capecitabine/ Capecitabine/Docetaxel Capecitabine/+Trastuzumab (not concomitant with Anthracyclines) Capecitabine with Lapatinib (who have received prior therapy including an Anthracycline, a Taxane, and Trastuzumab resistant)	Tamoxifen, LH-RH agonist + Tamoxifen, oophorectomy + Tamoxifen, Aromatase inhibitors restricted to FSH/LH/Estradiol levels compatible with postmenopausal status*	FAC/AC/taxane/Taxane Gemcitabine/ Cisplatin Vinorelbine/ Vinorelbine Capecitabine/ Capecitabine/ Docetaxel Capecitabine	Tamoxifen, LH-RH agonist + tamoxifen, oophorectomy + tamoxifen, Aromatase inhibitors restricted to FSH/LH/Estradiol levels compatible with postmenopausal status*	FAC/AC/taxane/Taxane Gemcitabine/Cisplatin Vinorelbine/ Vinorelbine Capecitabine/ Capecitabine/Docetaxel Capecitabine/CMF/Liposomal doxorubicin (restricted to EF borderline) Tamoxifen, LH-RH agonist +Tamoxifen, oophorectomy +Tamoxifen, Aromatase inhibitors restricted to FSH/LH/Estradiol levels compatible with postmenopausal status

* The levels are non-obligatory guiding criteria for the menopausal status of the patient.

* HR+: no proof of use of AI + LHRH > to tamoxifen +/- LHRH.

* HER+: Trastuzumab to be continued till progression of disease.



Postmenopausal Metastatic Breast Cancer

HR- HER-	HR- HER+	HR+ HER+	HR+ HER-
FAC/AC/Taxane/Taxane Gemcitabine/Cisplatin Vinorelbine/ Vinorelbine Capecitabine/Capecitabine/ Docetaxel Capecitabine/ CMF/ Liposomal Doxorubicin (restricted to decreased EF)	FAC/AC/taxane/Taxane Gemcitabine/ Cisplatin Vinorelbine/ Vinorelbine Capecitabine/ Capecitabine/ Docetaxel Capecitabine/ +Trastuzumab (not concomi- tant with Anthracyclines)/ capecitabine with Lapatinib (who have received prior therapy including an Anthracycline, a Taxane, and Trastuzumab resistant)	tamoxifen / aromatase inhibitor +/- trastuzumab	Tamoxifen, aromatase inhibitor (Letrozole, Anastrozole), in first and second line, Exemestane in third line after second line AI

* HR+: Aromatase inhibitors are slightly superior to tamoxifen.
 * HER+: Trastuzumab to be continued till progression of disease.

Adjuvant Therapy for HER+

TUMOR < 5 mm



No standard recommendation
based in clinical trials

TUMOR ≥ 5 mm



Chemotherapy + trastuzumab
for one year

- EC/ACx4 TH* x4 then H maintenance for a total of 1 year (18 doses combined and alone).
- FAC/FECx3 TH» x3 the H therapy for a total of 1 year.
- TCH x6 then H maintenance.

* (Docetaxel x 4 or paclitaxel weekly x 12)

» (Docetaxel x 3 or paclitaxel weekly x 12)

TCH = Docetaxel + carboplatin + trastuzumab

If trastuzumab is not available for one year, the Finher regimen might be an alternative (9 weekly administration of trastuzumab in combination with docetaxel followed by FE (60)C Hormonal therapy if HR positive expression)



Adjuvant Therapy for HER-

Luminal A
(HR +strongly positive in more than 70% of the cells, grade 1,
low proliferative index <10%)

.....● Endocrine therapy*/Chemotherapy (to be considered if adverse prognostic factors are present) followed by Endocrine therapy*

Luminal B
Node Negative

.....● AC x 4 (TC x 4 in patients with cardiac risk - EF<50%)

Node Positive:

.....● FEC/FAC x 6
3 FEC → 3 Docetaxel
4 AC → 4 Docetaxel or weekly paclitaxel x 12
TC x 6 (in patients with cardiac risk - EF<50%)
FAC/FEC → CMF
TAC* and dose dense ACT in selected patients: young patients, highly proliferative tumors).

* Taxotere, Adriamycin and cyclophosphamide (risk of hematological toxicity, G-CSF mandatory).

Adjuvant Hormone Therapy

HR+ disease / premenopausal

- Hormone therapy Tamoxifen, LHRH agonist may be considered for women 40 years or less.
- Administration of chemotherapy and hormonal therapy: sequential therapy is the standard schedule.
- Combination of LHRH agonist and aromatase inhibitor not proven to be superior to tamoxifen +/- LHRH for 2-3 years.

HR+ disease post menopausal

- Hormone therapy: Aromatase inhibitor for 2-3 years followed by tamoxifen for 2-3 years (total 5 years) or Aromatase inhibitor for 5 years seems superior for luminal B patients (ER <80%) with a high Ki 67 index (>14%) while tamoxifen is equivalent in luminal A (ER >80%) Ki <14%

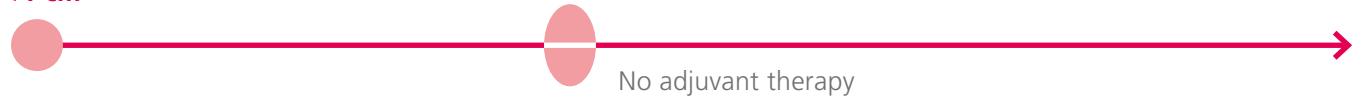


Adjuvant Therapy

→ Zoledronic acid in the adjuvant setting only in the case of documentation of osteoporosis/ osteopenia (category IIB).

Tubular and Colloid Histology, Node Negative

T < 1 cm



T > 1 cm



Node positive



04 Epithelial Ovarian and Endometrial



Epithelial Ovarian Carcinoma (EOC)

Recurrent Epithelial Ovarian Carcinoma

Metastatic Endometrial Cancer

Recurrent Endometrial Cancer

Clear Cell Endometrial Cancer

Uterine Papillary Serous Cancer (UPSC)

Cervical Cancer



Epithelial Ovarian Carcinoma (EOC)



Early EOC

High risk group
adequate complete staging followed by chemotherapy, the standard of care consists of 6 cycles of intravenous paclitaxel 175 mg/m² over 3 hours followed by i.v. carboplatin every 3 weeks

Low risk group
adequate complete staging followed by observation without chemotherapy

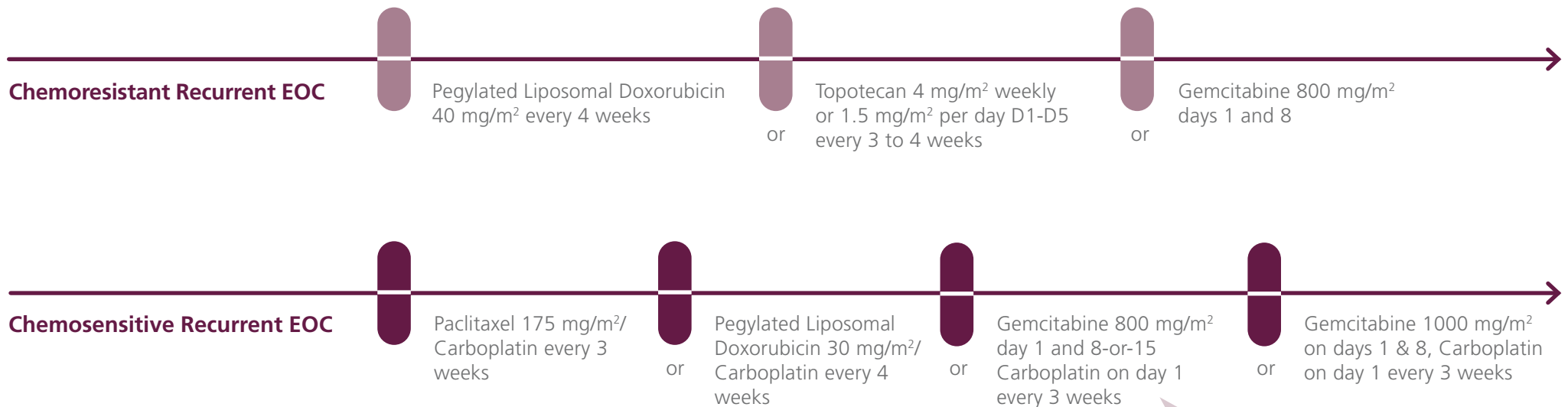
Advanced EOC

Aggressive surgical bulk reduction
(tumor residual < 1 cm, preferably R0, including aggressive upper abdominal surgery and bowel and liver resection if needed and safely performed) followed by chemotherapy

Standard chemotherapy
consisting of intravenous Paclitaxel 175 mg/m² over 3 hours followed by i.v. carboplatin with the combination given every 3 weeks for 6 cycles

Newly evolving standard of care
intraperitoneal chemotherapy with Cisplatin and Paclitaxel every 3 weeks in patients with small-volume residual disease after maximal surgical bulk reduction.

Recurrent Epithelial Ovarian Carcinoma



Treatment should be continued until progression of disease, unacceptable toxicity, or achievement of a clinical complete response. If a patient achieves a clinical complete remission on therapy and experiences a reasonable (i.e., greater than 6 months) treatment-free interval before recurrence, retreatment with a carboplatin-based doublet should produce the best results. Repetitive treatment should continue until the patient becomes chemoresistant, and only then should alternative nonplatinum regimens be considered.



Metastatic Endometrial Cancer

Chemotherapy-naive with good performance status

→ Treat with combination chemotherapy.

A combination of Paclitaxel, Doxorubicin, and Cisplatin has shown the highest overall response rates to date.

A combination of Paclitaxel and Carboplatin is also effective and potentially less toxic.

In women with multiple medical comorbidities

→ single-agent chemotherapy may be better tolerated with acceptable results.

In women with low grade tumors and/or in women with a poor performance status

→ Hormonal therapy should be considered

Recurrent Endometrial Cancer



Patients with hormone-sensitive tumors (positive receptor levels, low-grade tumors, and long disease-free interval)

- Megestrol (160-200 mg) as first-line
- Tamoxifen as second-line



Patients with high-grade tumors, negative hormone receptor levels, and short treatment-free interval

- Paclitaxel, Doxorubicin, and Cisplatin are the most active but with significant toxicity.

In phase II studies, the combination therapy with Paclitaxel and Carboplatin seems to be as effective but less toxic and can be administered in outpatient clinic.



Clear Cell Endometrial Cancer

-● **Comprehensive surgical staging**
including simple hysterectomy, bilateral salpingo-oophorectomy, pelvic, para-aortic lymphadenectomy, omentectomy and cytologic evaluation of the abdominal/pelvic peritoneum should be performed to allow for planning of appropriate adjuvant treatment and surveillance.
-● **Platinum based adjuvant chemotherapy**
in a doublet or triplet format in combination with Paclitaxel and/or Doxorubicin should be considered in women presenting with extra-uterine disease.

Similar regimens can be utilized in women with recurrent disease.
-● Given the relatively high incidence of distant recurrence of disease, use of adjuvant treatment with platinum-based chemotherapy may be reasonable in women diagnosed with stage I and II disease.
-● **Careful long term surveillance**
following treatment is indicated

Uterine Papillary Serous Cancer (UPSC)

-● **Surgical staging**
should be performed when feasible. In addition to simple hysterectomy, bilateralsalpingo-oophorectomy, pelvic and paraaortic lymphadenectomy, and washings for cytology, performance of omentectomy and peritoneal biopsies should be considered.
-● **Adjuvant therapy**, including platinum-based chemotherapy and vaginal brachytherapy, should be considered in women with stage I.
-● Women with advanced-stage disease are best treated with optimal cytoreduction of metastatic disease followed by adjuvant platinum-based chemotherapy (Carboplatin and Paclitaxel or Cisplatin and Doxorubicin).
-● **Careful long term surveillance**
following treatment is indicated

The relatively favorable prognosis of women with stage IA UPSC with no residual uterine disease after comprehensive surgical staging may justify close observation alone. However, **adjuvant chemotherapy and vaginal brachytherapy** should be considered in other stage IA patients.

Cervical Cancer



05 Gastrointestinal



Colon Cancer

Rectal Cancer

Pancreatic Cancer

Biliary and Gallbladder Cancer

Esophageal Carcinoma

Hepatocellular Carcinoma

Small Intestine Carcinoma

Gastric and GE Junction Carcinoma

Gastrointestinal Stromal Tumor



Colon Cancer Adjuvant

Single Agent

1 5-FU + Leucovorin

Mayo Protocol

5 days/M for 6 months

Park Protocol

weekly for 6 weeks then 2 weeks off i.e. Q 8 h for a total of 6 M

de Gramont protocol

infusional 5-FU + Ca folinate for 48 h Q 2 weeks for 6 months

2 Capecitabine (Xeloda)

up to 6 months (recommended for elderly >75 years old or patients unfit for IV combination chemotherapy)

Combination Chemotherapy (Oxaliplatin + 5FU And LLV)

1 FOLFOX

Stage III & high risk Stage II
high risk Stage II*

2 Flox Protocol

Stage III & T4
Stage III & high risk Stage II*

3 XELOX

Oxaliplatin+Capecitabine every 3 weeks for 6 months
Stage III & high risk Stage II*

* High risk stage II includes patients with perforation, poorly differentiated tumors, T4 lesions, understaged with less than 12 lymph nodes at the time of surgery

Colon Cancer Advanced

evaluation every 2-3 months

First Line Regimens

FOLFOX and Bevacizumab

(phase III data with modest improvement in progression free survival; study thought to have many limitations)

FOLFIRI and Bevacizumab

(acceptable regimen without phase III data at this point)

FOLFIRI and Cetuximab

(Phase III data with PFS and OS benefit in wild type KRAS patients)

Second Line Regimens

If patient had FOLFOX in first line, then use irinotecan based regimen

If patient had FOLFIRI in first line, then use FOLFOX

For mutant KRAS patients

If patient received Bevacizumab in first line, give chemotherapy alone in second line; if not, then add Bevacizumab to chemotherapy in second line

→ Single agent

- 1 5-FU + Leucovorin ± targeted therapy (push or infusional weekly or biweekly)
- 2 Capecitabine ± targeted therapy
- 3 Irinotecan

→ Combination chemotherapy

- 1 FOLFOX (or XELOX) ± targeted therapy
- 2 FOLFOX (modified) ± targeted therapy
- 3 FOLFIRI ± targeted therapy

For wild type KRAS patients

→ If patient had received Bevacizumab in first line, then use second line chemotherapy alone or chemo+EGFR antibody (Cetuximab)

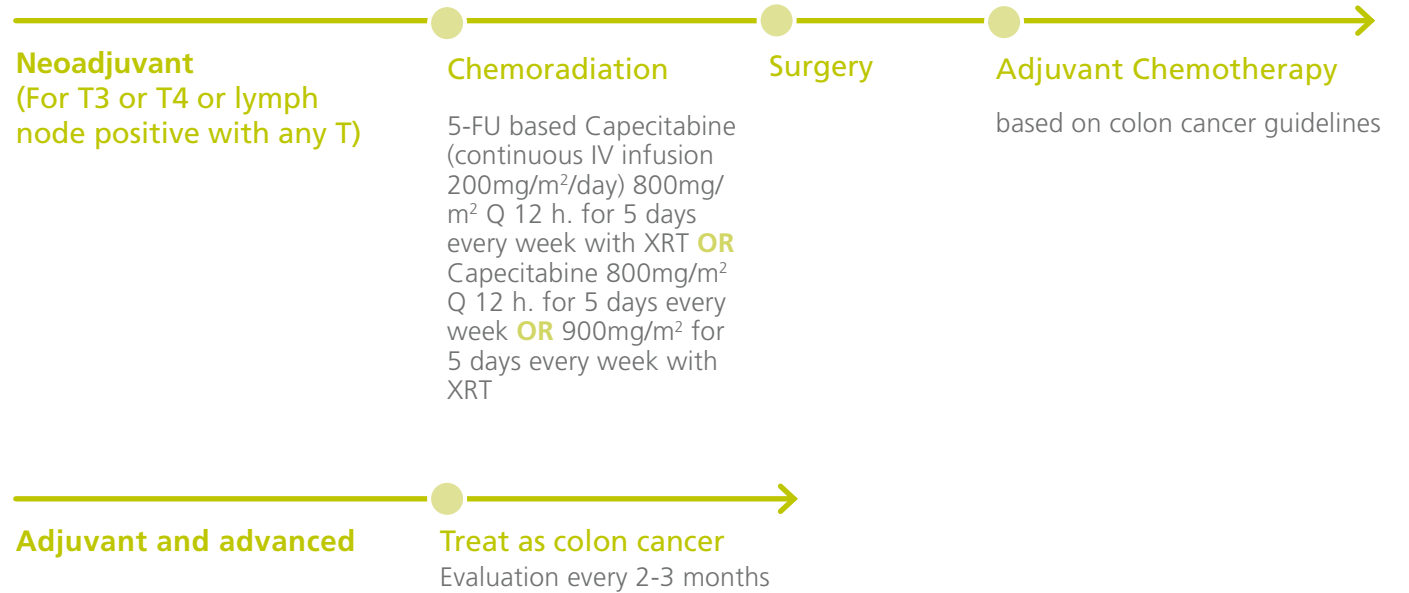
→ If patient did not have Bevacizumab in first line, then add Bevacizumab to chemotherapy in second line.

→ It is acceptable not to use a targeted agent in second line for patients who are asymptomatic with a good performance status, as they may receive anti-EGFR therapy in third line (alone or with irinotecan)

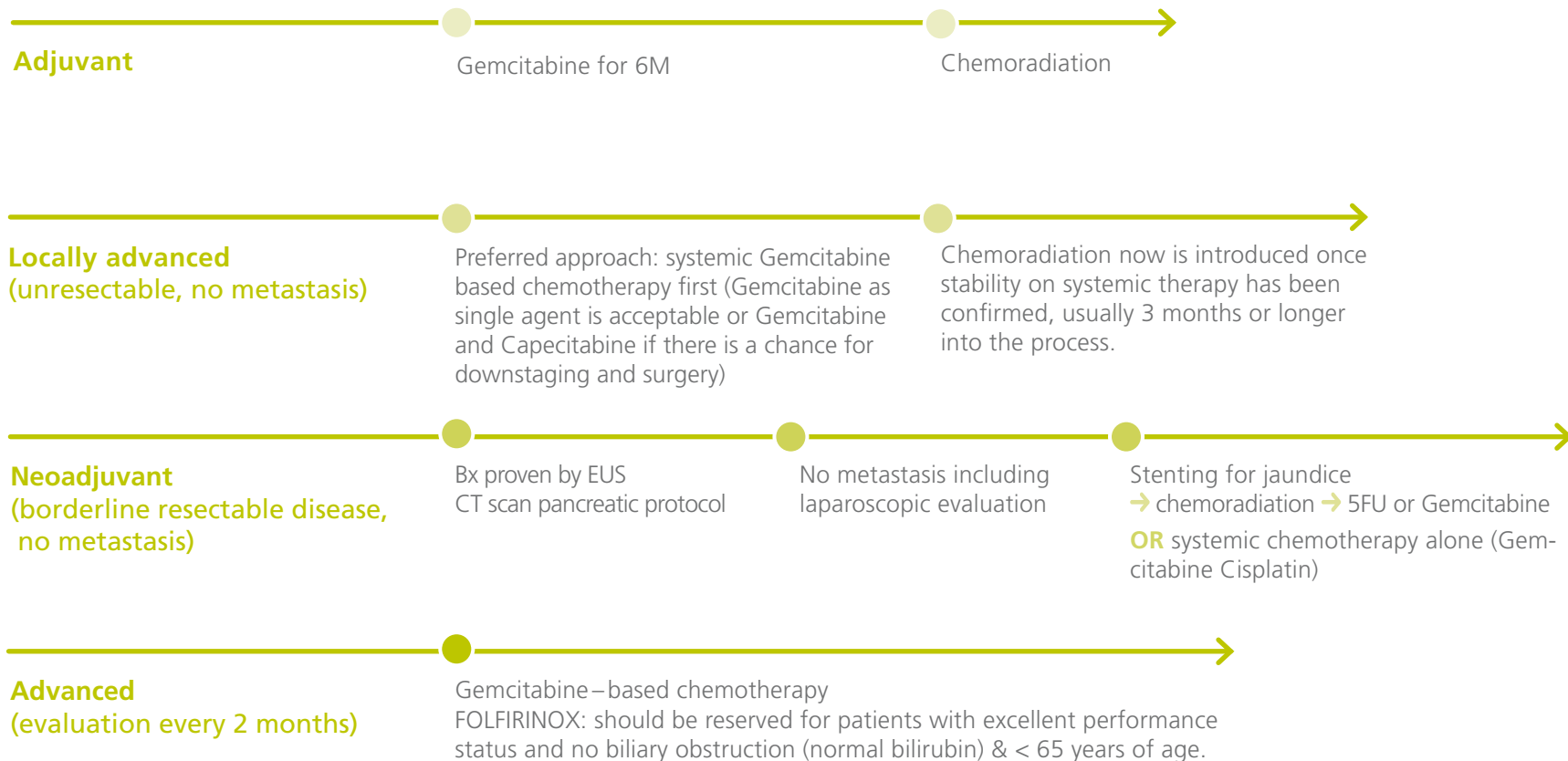
→ Targeted therapy: Bevacizumab (Avastin) or Cetuximab (Erbix)



Rectal Cancer

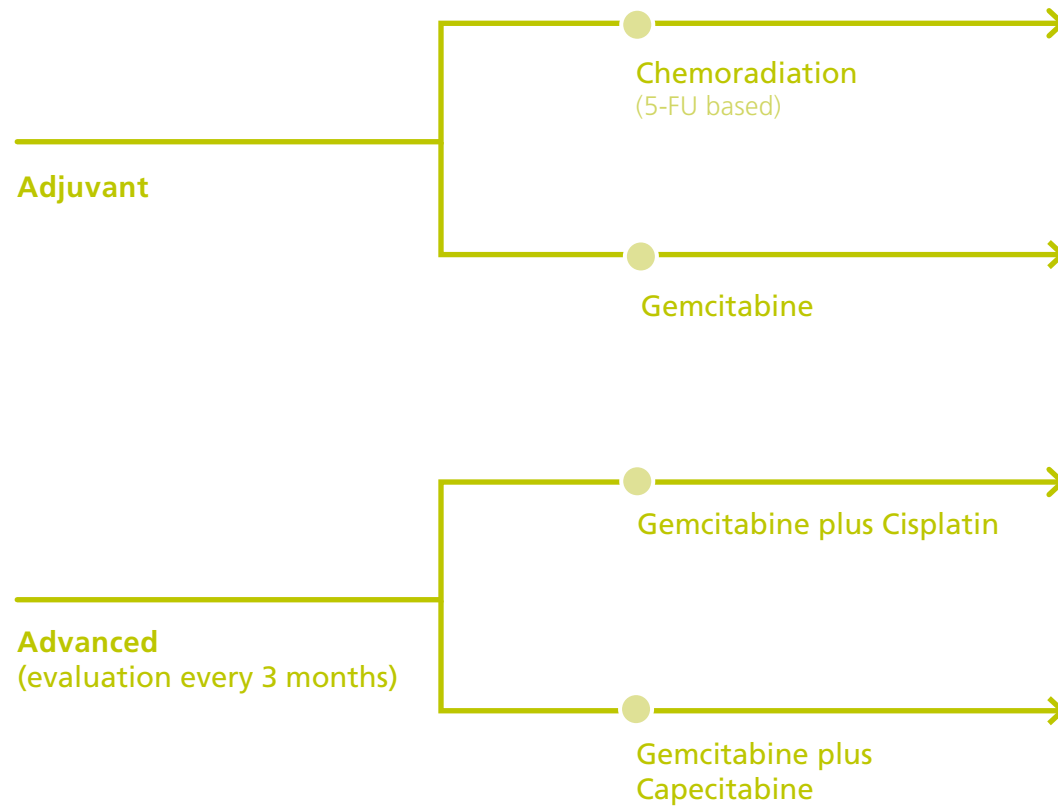


Pancreatic Cancer

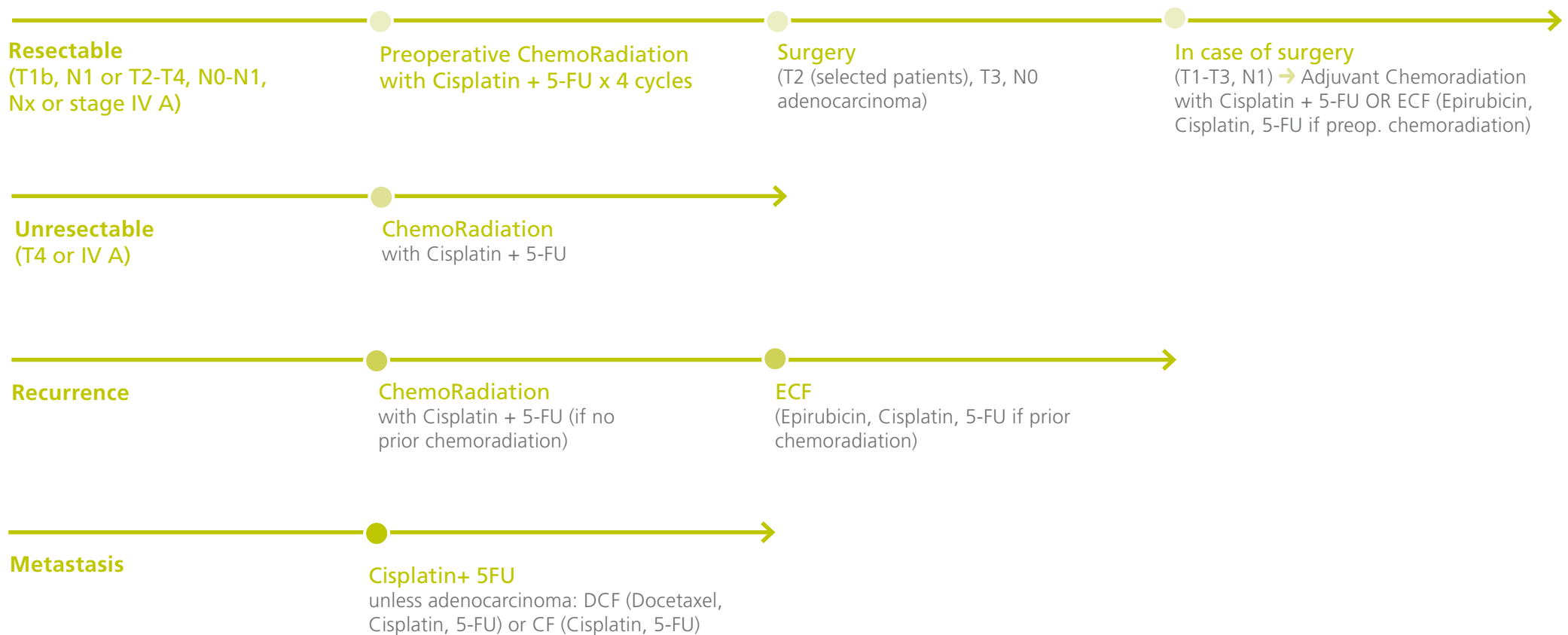




Biliary and Gallbladder Cancer



Esophageal Carcinoma





Hepatocellular Carcinoma

Would recommend following BCLC staging and treatment recommendations

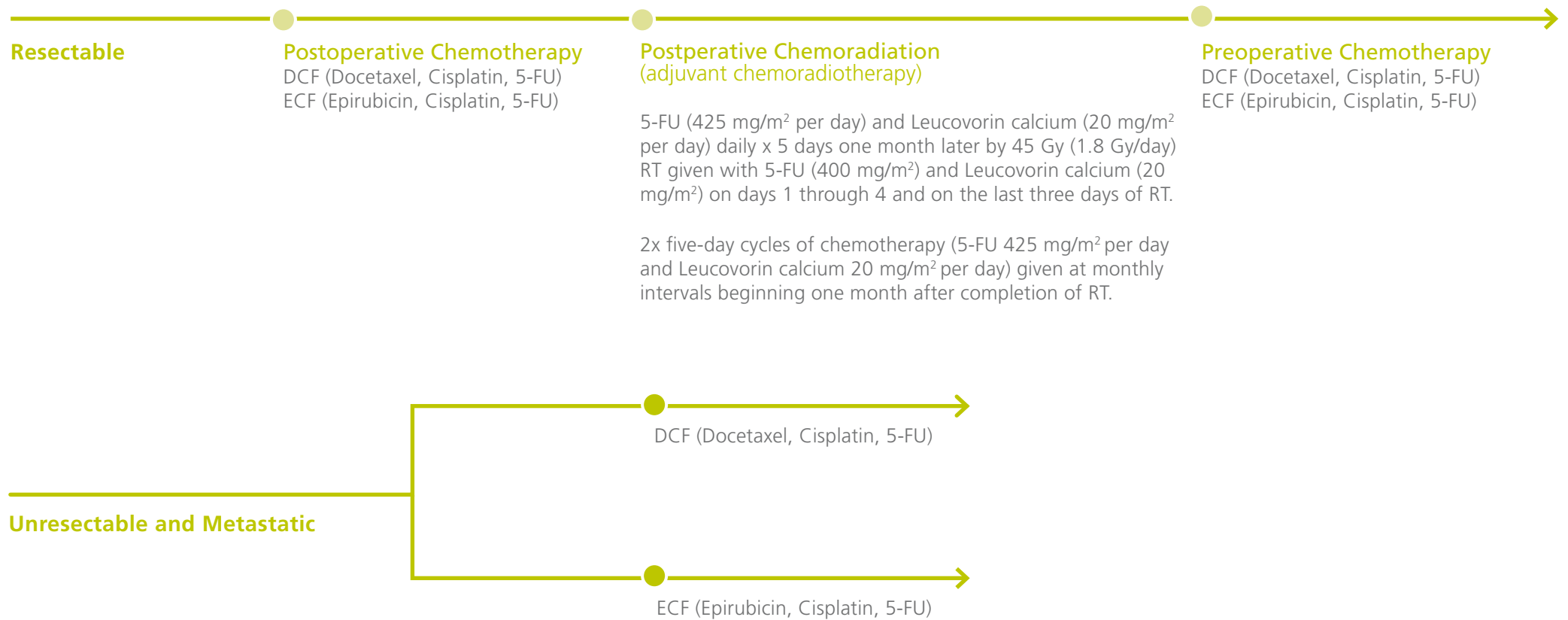
Localized unresectable → Chemoembolization (Doxorubicin)

Sorafenib for metastatic hepatocellular carcinoma excluding Child-Pugh Class C disease

Small Intestine Carcinoma

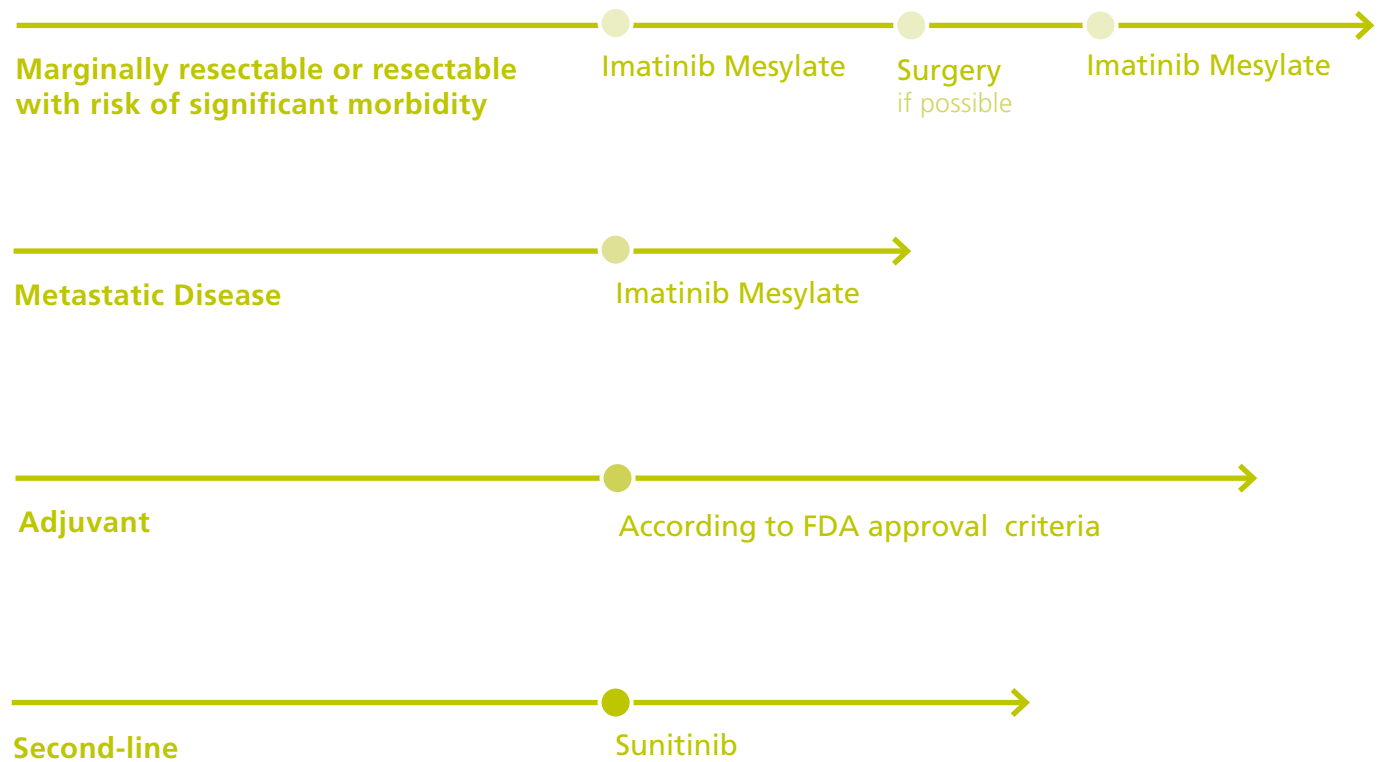


Gastric and GE Junction Carcinoma





Gastrointestinal Stromal Tumor



06 Urogenital tumors and Soft Tissue Sarcomas



Urothelial tumors

Non-Seminomatous Germ Cell Tumors

Seminoma

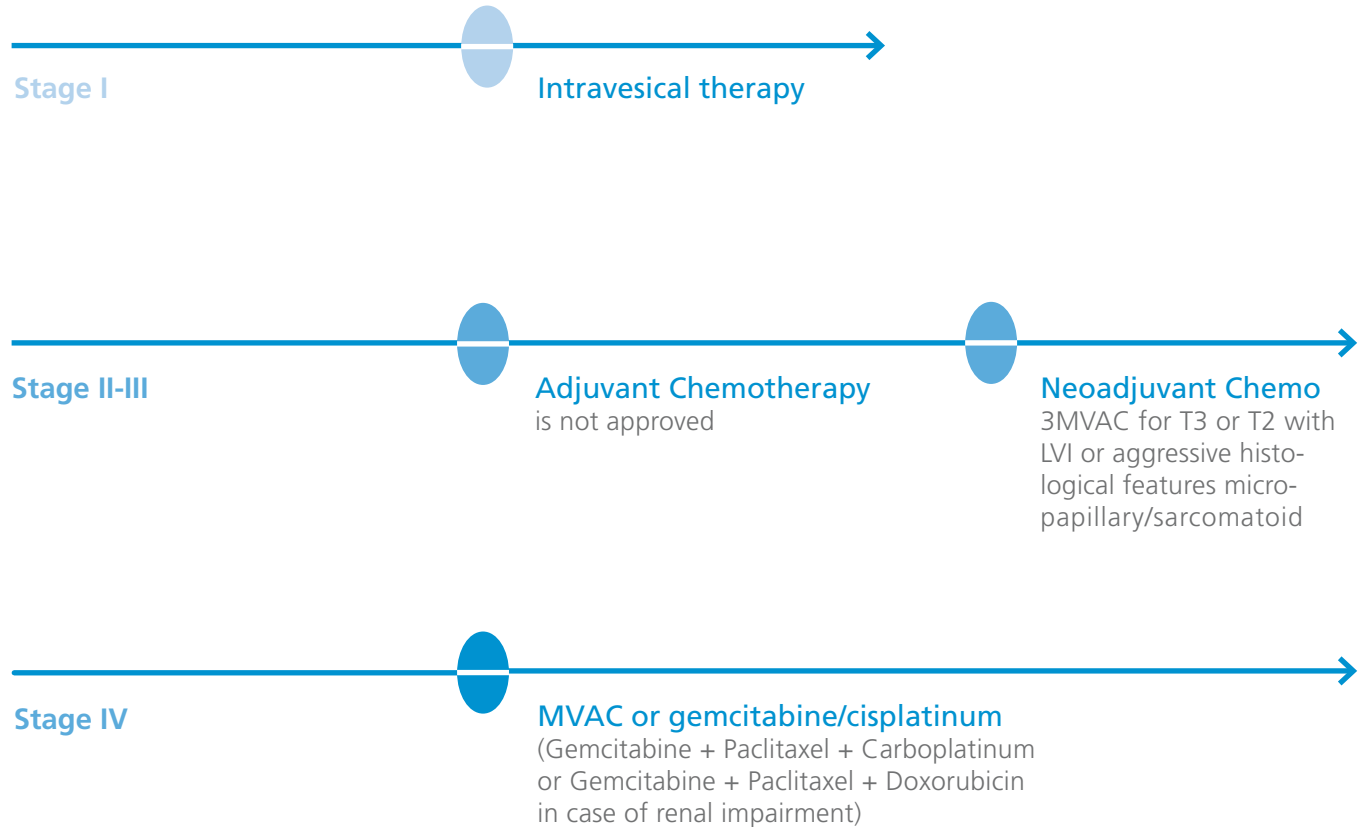
Renal Cell Carcinoma

Prostate Cancer

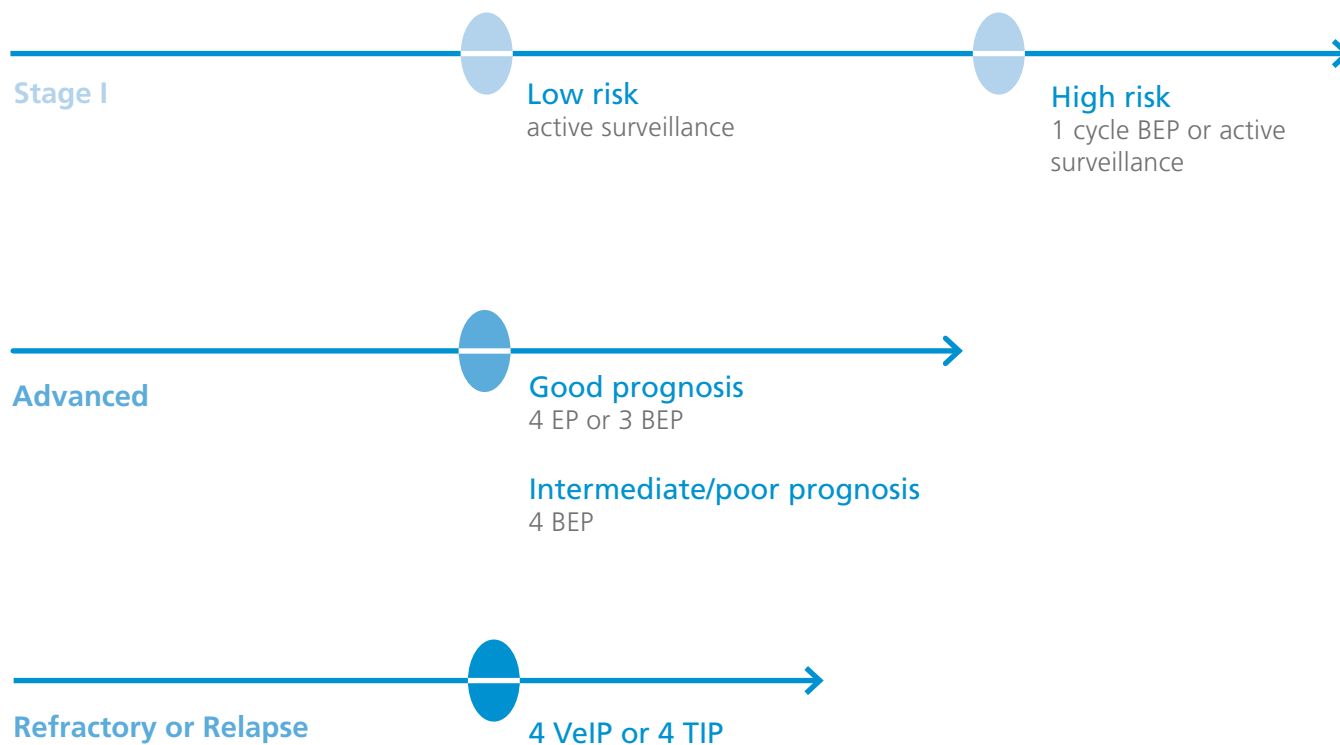
Soft tissue sarcoma
(limbs, retroperitoneum, pelvis)



Urothelial Tumors



Non-Seminomatous Germ Cell Tumors





Seminoma


Stage I
RT or 1 cycle of carboplatin or active surveillance

Stage II A/B
RT

Stage II C/III
4 BEP

Renal Cell Carcinoma

Completely resected




No adjuvant therapy

Unresectable or
Metastatic, clear cell
carcinoma excluding the
sarcomatoid type



Good/intermediate risk
Sunitinib 50 mg/d 4/6 weeks
or 37.5 mg p.o. daily

Metastatic sarcomatoid renal
cell carcinoma



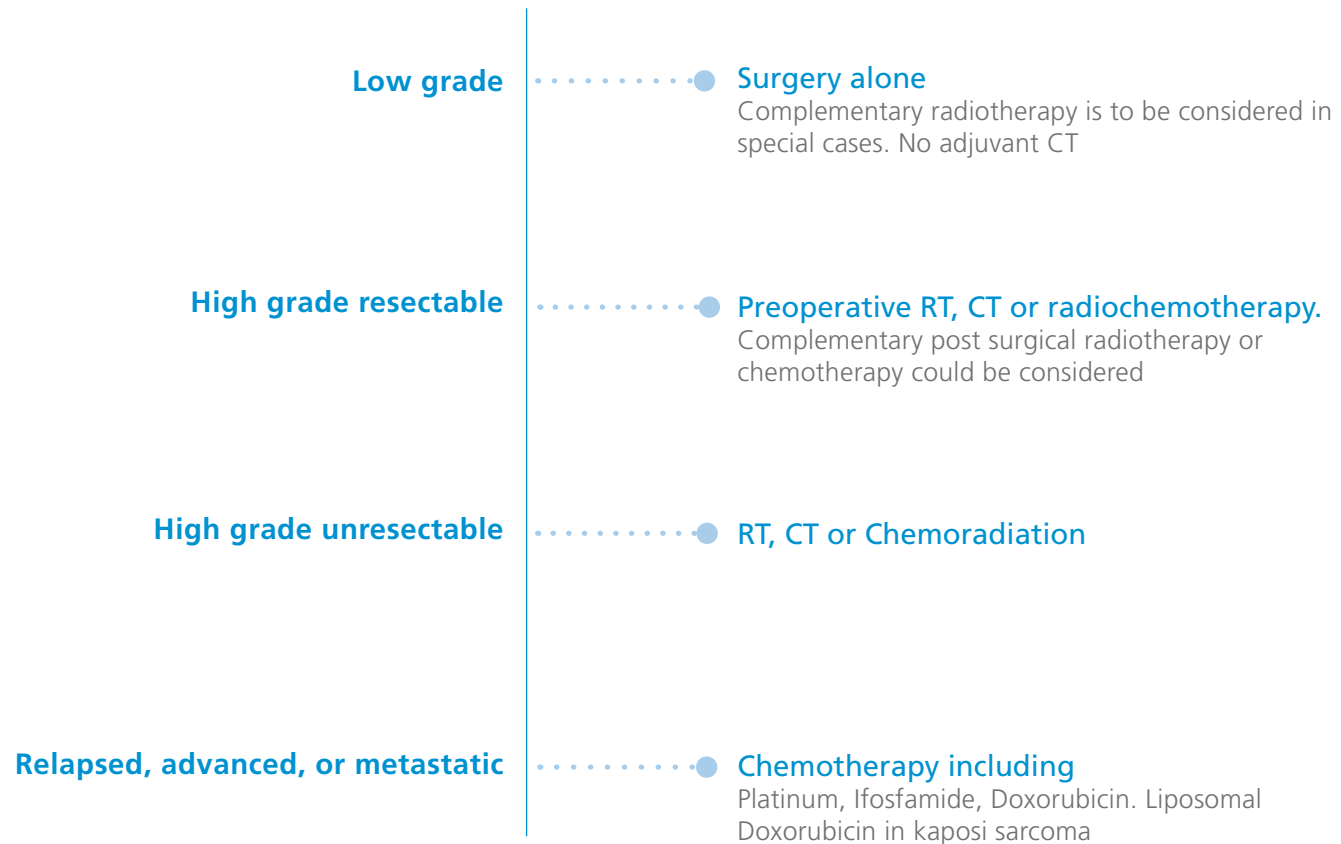
gemcitabine + doxorubicin



Prostate Cancer

Localized	● Surgery Or Radiotherapy Androgen deprivation could be indicated in sandwich with radiotherapy in T2-T4
Metastatic, Hormone Sensitive	● Surgical Or Medical Castration 4 weeks antiandrogen is indicated before medical castration
Bone Metastasis	● Biphosphonates
Metastatic, Hormone Resistant	● first-line Docetaxel + Prednisone second-line Cabazitaxel + Prednisone (less than 70 years old, performance status less than 2)

Soft Tissue Sarcoma (Limbs, Retroperitoneum, Pelvis)



07 Hematology Guidelines 2012



Diffuse Large B Cell Non Hodgkin's
Lymphoma (CD20+)

Diffuse Large B Cell Lymphoma (CD20+)

Low grade non Hodgkin's
lymphoma (CD20+)

Hodgkin's lymphoma

Acute Myeloblastic Leukemia

Age < 65 years (except promyelocytic Leukemia)

Acute Myeloblastic Leukemia

Age > 65 years (except promyelocytic Leukemia)

Acute Promyelocytic Leukemia (APL)

B Chronic lymphocytic leukemia

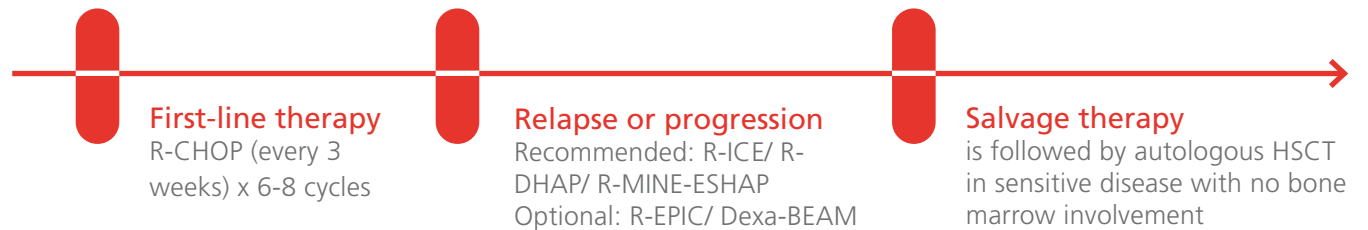
Chronic Myelogenous Leukemia (CML)

Myelodysplastic Syndromes

Multiple Myeloma



Diffuse Large B Cell Non Hodgkin's Lymphoma CD20+, Age < 65 years



Diffuse Large B Cell Lymphoma CD20+, Age > 65 years



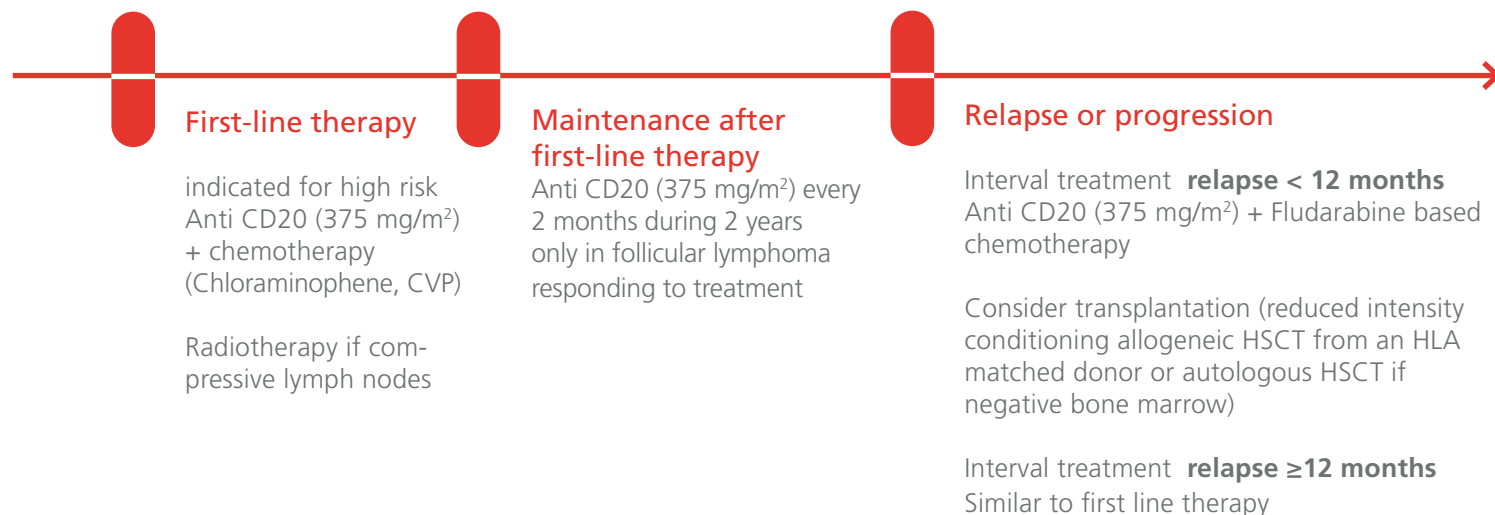
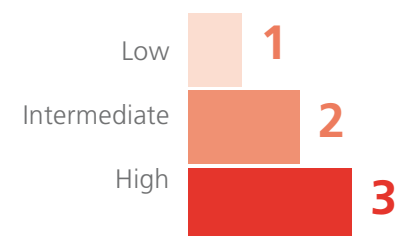


Low Grade Non Hodgkin's Lymphoma (CD20+)

Prognostic Factors (FLIPI)

Age ≥ 60 y
Stage Ann Arbor Stage III-IV
Hb < 12 g/dL
LDH $>$ Upper limit of normal
Number of nodes sites ≥ 5

Risk Group Number of Factors



Hodgkin's Lymphoma

Early stage (I, II)

Without unfavorable factor(s)
ABVD (2 cycles) followed by involved field radiotherapy (20 to 30 Gy)
if ABVD not feasible consider COPP

With unfavorable factor(s)
ABVD (4 cycles) followed by involved field radiotherapy (30 Gy)
if ABVD not feasible consider COPP

Radiotherapy alone could be proposed for stage IA nodular lymphocyte predominant type

Chemotherapy
ABVD (6 to 8 cycles)
BEACOPP regimen could be considered in selective cases
if ABVD or BEACOPP not feasible consider COPP

Radiotherapy
on residual mass and/or initial bulk



Hodgkin's Lymphoma

Progression or Relapse

If primary therapy is radiotherapy alone
treatment as an advanced disease

If primary therapy is chemotherapy ± radiotherapy

Salvage non cross resistant chemotherapy: ICE / IVE/ ASHAP/ MIME/ Dexamethasone-BEAM/ Ifosfamide + Vinorelbine, gemcitabine, followed by autologous HSCT in sensitive disease

Relapse After Autologous HSCT

< 6 months
Supportive care

> 6 month
Salvage chemotherapy followed by reduce intensity conditioning from an HLA matched donor if sensitive or stable disease



Unfavorable Factors

ESR \geq 50

Bulky disease

mediastinal mass > 35% of the thoracic diameter

any other mass > 10 cm

B symptoms and ESR \geq 30

> 3 sites

Extranodal sites

Acute Myeloblastic Leukemia except Promyelocytic Leukemia

Diagnosis Age ≤ 60 y

Specific Tests

Bone marrow aspirate (or blood if circulating blasts) for

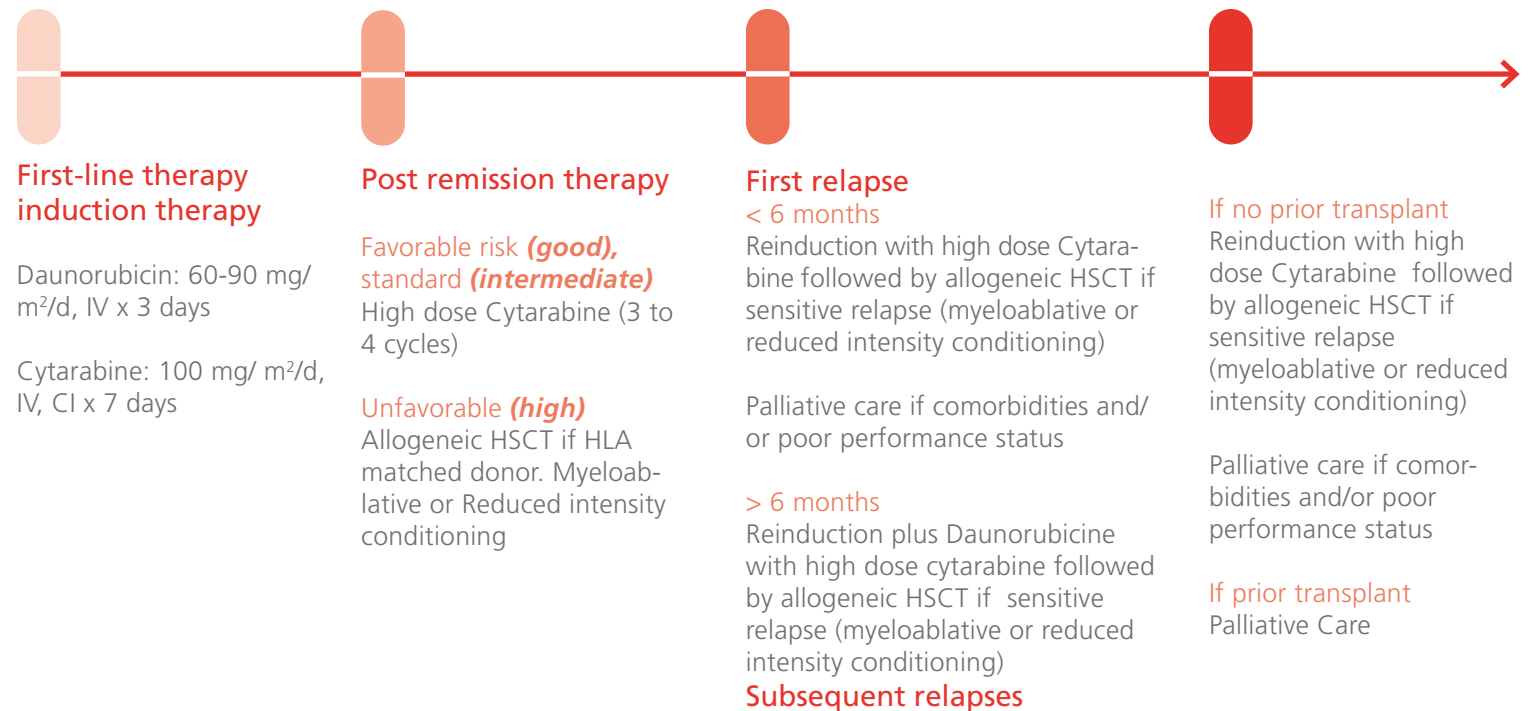
- Cytology
- Flow Cytometry (Immunophenotyping)
- Chromosomal analysis by
 - Conventional karyotype T(≥20 fully analyzed metaphase cells)
 - FISH for inv16, t(8;22), t(15;17)
- Molecular biology is an optional test

Prognostic Factors

Risk	Favorable (<i>good</i>)	Intermediate (<i>standard</i>)	Unfavorable (<i>high</i>)
Chromosomal Abnormality	<ul style="list-style-type: none"> → t(8;21) (q22;q22) t(15,17) → inv16 (p13q22)/t(16;16) (p13;q22) → t(8,21) without del(9q) or complex karyotype 	<ul style="list-style-type: none"> → Normal Karyotype → t(9;11)(p22 ;q23) del(7q)- del(9q) -del(11q)- del(20q) -Y, +8, +11, +13, +21 	<ul style="list-style-type: none"> → Complex karyotype → Inv(3)(q21q26)/t(3;3)(q21;q26) t(6;9)(p23;q34) t(6;11)(q27;q23) t(11;19)(q23;p13.1) t(9,22) del(5q)-5, -7 abnormal 17p >1 cycle of induction to obtain CR → t(8,21) with del(9q) or complex karyotype
Genetics Alteration		<ul style="list-style-type: none"> → With no genetic alteration → Favorable: NPM1 mutation/FTL3- ITD- CEBPA mutation → Unfavorable: FLT3-ITD+MLL-PTD BAALC overexpression ERG overexpression 	

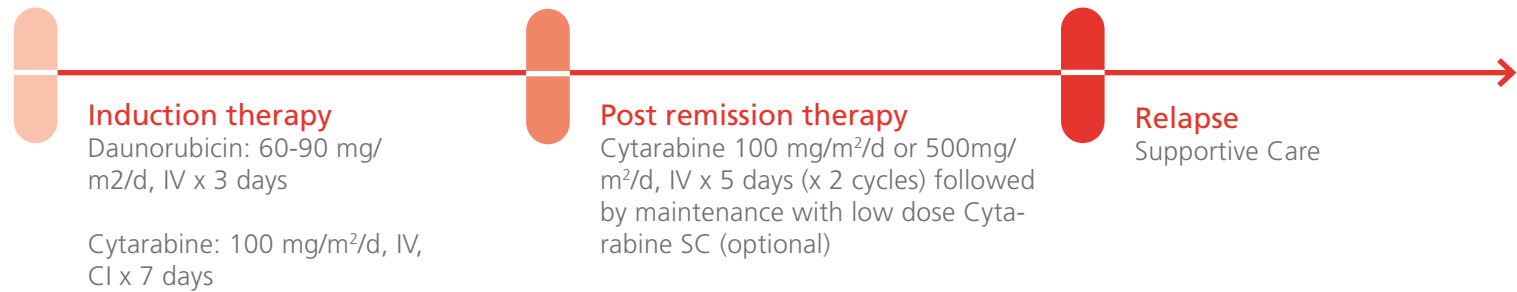


Acute Myeloblastic Leukemia age \leq 60 years, except Promyelocytic Leukemia

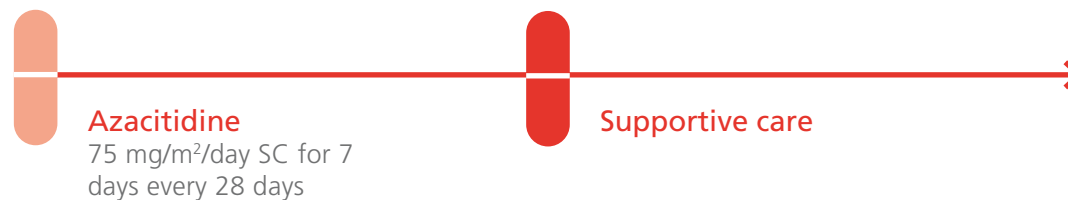


Acute Myeloblastic Leukemia

60 ≤ age ≤ 70 years, except Promyelocytic Leukemia



age > 70 years





Acute Promyelocytic Leukemia (APL)



Induction, Low Risk (WBCs <10,000):

ATRA 45 mg/m² PO (divided in two daily doses) until repeat BM shows CR

Arsenic trioxide 0.15 mg/kg over 1 hour daily until repeat BM shows CR

***May add Idarubicin if hyperleukocytosis develops on treatment**

Induction, High Risk (WBCs >10,000):

ATRA 45 mg/m² PO (divided in two daily doses) until repeat BM shows CR

Arsenic trioxide 0.15 mg/kg over 1 hour daily until repeat BM shows CR

Idarubicin 12 mg/m² IVPB on day 1. [may substitute Daunorubicin if Idarubicin is not available]



Consolidation

8 months of therapy consisting of ATRA 2 weeks on, 2 weeks off and Arsenic trioxide every other month. Specifically:

ATRA 45 mg/m² PO (divided in two daily doses) for 14 days of each month for 8 months.

Arsenic trioxide 0.15 mg/kg over 1 hour daily 5 days weekly for 4 weeks (total of 20 doses), every other month for 8 months.



Monitoring

If available, consider PCR monitoring.

If negative

As above and repeat every 3 months. If positive, repeat 1-3 weeks later.

If confirmed

Add Idarubicin 6 mg/m²/day x 2 doses to ATRA + Arsenic until PCR is negative.



B Chronic Lymphocytic Leukemia

Diagnosis

Specific tests

CBCD, Platelets

Bone marrow aspirate (or blood) for

- Cytology
- Flow cytometry (Immunophenotyping)
(CD5, CD10, CD19, CD20, CD23, CD38, Kappa/ Lambda)

Chromosomal analysis by

- Karyotype
- FISH (if possible) to detect t (11;14), del(17p), del(13q), +12, del(11q)

Prognosis

	↓	→	↑
	Unfavorable	Neutral	Favorable
T(11q,v)		Normal	del (13q)
del (11q)		+12	Normal
del (17p)			
CD38 > 30%			CD38 < 30%
ZAP – 70 > 20%			ZAP – 70 < 20%
IgVH mutation ≤2%			IgVH mutation > 2%
p53 (mutation or deletion)			

Staging

	■	■	■
Risk	Good	Intermediate	High

Rai System	0,I	II,III	IV
------------	------------	---------------	-----------

Binet System	A	B	C
--------------	----------	----------	----------

First line therapy

Asymptomatic patients should be monitored regularly

Indication for treatment

Presence of symptoms
Autoimmune cytopenia
Recurrent infections requiring hospitalization more than 2 times during the last 6 months
Bulky disease
Rai high risk
Binet C

Treatment

Age < 65, Kps > 80*
(younger, medically fit)

Fludarabine +
Cyclophosphamide
Rituximab (FCR)
R-CVP
CVP
Fludarabine + Cyclophosphamide (FC)

Age > 65, Kps < 80*
(older, medically less fit)

Chlorambucil
CVP
FC

*Karnofsky performance score

Relapse or Progression

Fludarabine + Cyclophosphamide +
Rituximab (FCR)
previously cited primary treatments

Allogeneic HSCT (mainly reduced intensity conditioning) from an HLA matched donor is considered if:

Non response or early relapse (within 12 months) after purine analogue containing therapy (eg: Fludarabine)

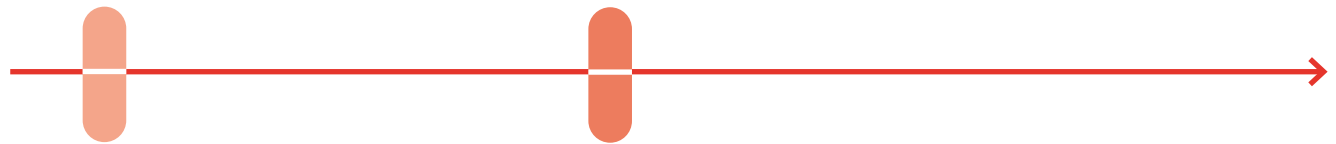
Relapse (within 24 months) after purine analogue-combination therapy (eg: Fludarabine based)

Mutation del(17p) or p53 (mutation or deletion)



Chronic Myelogenous Leukemia (CML)

Newly diagnosed chronic phase CML



First line

Imatinib 400mg daily.
Continue treatment in case of optimal response¹.

¹Optimal response is defined as:
Obtaining complete hematological response at 3 months
At least partial cytogenetic response at 6 months
Complete cytogenetic response at 12 months
Complete molecular response at 18 months
Stable or improving MMR.

Second line

In case of Imatinib toxicity, intolerance or failure² use second generation TKI: Dasatinib or Nilotinib.

²Failure is defined as:
Less than CHR at 3 Mo
No CgR at 6 Mo
Less than PCgR at 12 Mo
Less than CCgR at 18 Mo
Loss of CHR, Loss of CCgR at any time

In case of suboptimal response³, continue imatinib same dose or test imatinib high dose; consider dasatinib, or nilotinib

³Sub optimal Response is defined as:
No CgR at 3 Mo
Less than PCgR at 6 Mo
PCgR at 12 Mo
Less than MMR at 18 Mo
Loss of MMR at any time

- Allo HSCT in patients who have experienced progression to AP/BP and in patients who carry the T315I mutation



Third line

In case of dasatinib or nilotinib suboptimal response, continue dasatinib or nilotinib, with an option for Allo HSCT.

In case of dasatinib or nilotinib failure, then consider Allo HSCT.

Accelerated Phase or Blastic Phase (AP, BP)



First line

Patients who are TKI naïve: TKI followed by Allo HSCT

Second line

Patients with prior treatment of imatinib: dasatinib or nilotinib followed by Allo HSCT

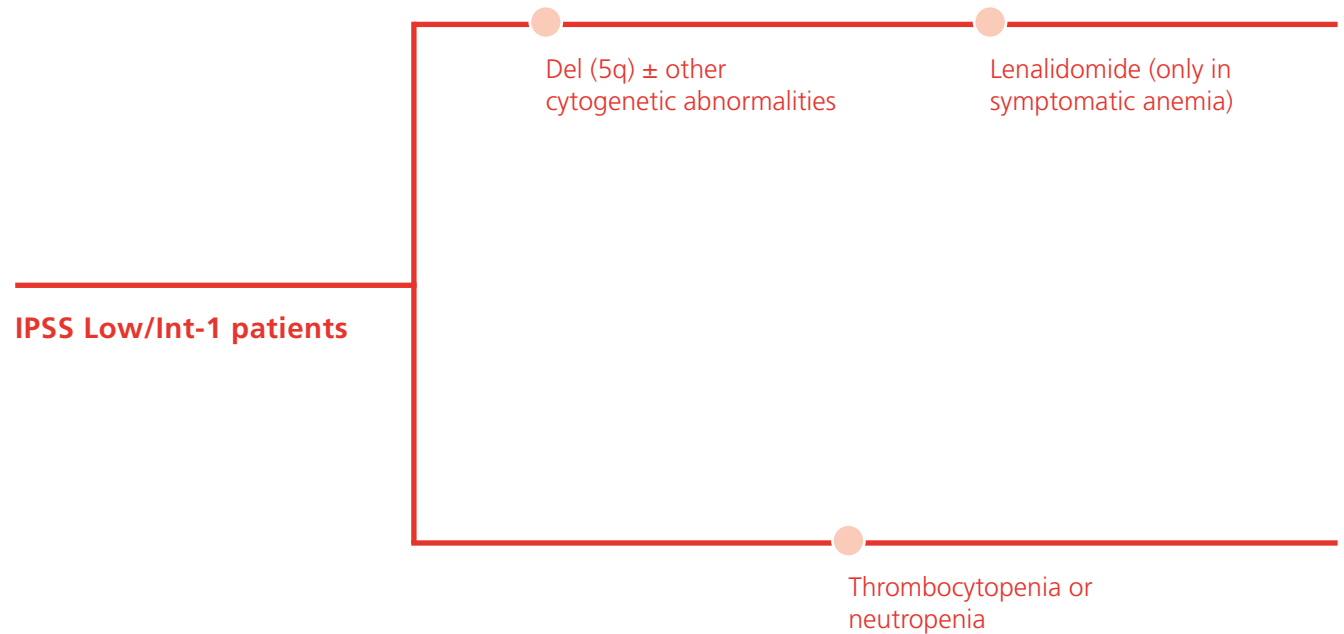
Remission definitions and monitoring

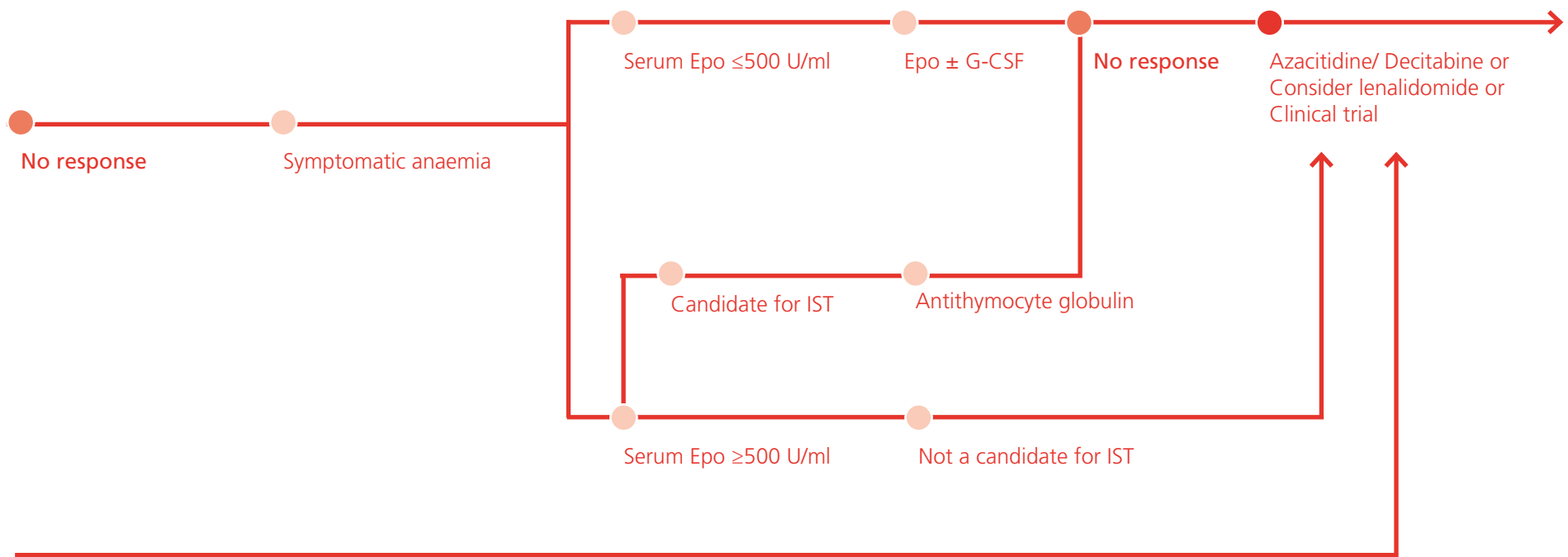
	Definition	Monitoring
Hematologic		
Complete (CHR)	Platelet count < 450 x 10 ⁹ /L WBC count < 10 x 10 ⁹ /L Differential: no immature granulocytes, basophils < 5% Non palpable spleen	Check at diagnosis, then every 15 days until CHR has been achieved and confirmed, then at least every 3 months or as required
Cytogenetic		
Complete (CCgR)	No Ph+ metaphases	Check at diagnosis, at 3 months, and at 6 months, then every 6 months until a CCgR has been achieved and confirmed, then yearly.
Partial (PCgR)	1-35% Ph+ metaphases	
Minor	36-65% Ph+ metaphases	
Minimal	66-95% Ph+ metaphases	
None	> 95% Ph+ metaphases	Check always for occurrences of treatment failure (primary or secondary resistances), and for occurrence of unexplained anemia, leukopenia, or thrombocytopenia.
Molecular		
Complete (CMR)	Undetectable BCR-ABL mRNA transcripts by real time quantitative and/or nested PCR in two consecutive blood samples of adequate quality (sensitivity > 10 ⁴)	RT-Q-PCR: Optional at diagnosis; Every 3 months, until MMR has been achieved and confirmed, then at least every 6 months.
Major (MMR)	Ratio of BCR-ABL to ABL (or other housekeeping genes) ≤ 0.1% on the international scale	Mutational analysis: In occurrence of suboptimal response or failure, always required before changing to other TKIs or other therapies.



Myelodysplastic Syndromes

Potential MDS treatment algorithm: Low-risk and Int-1

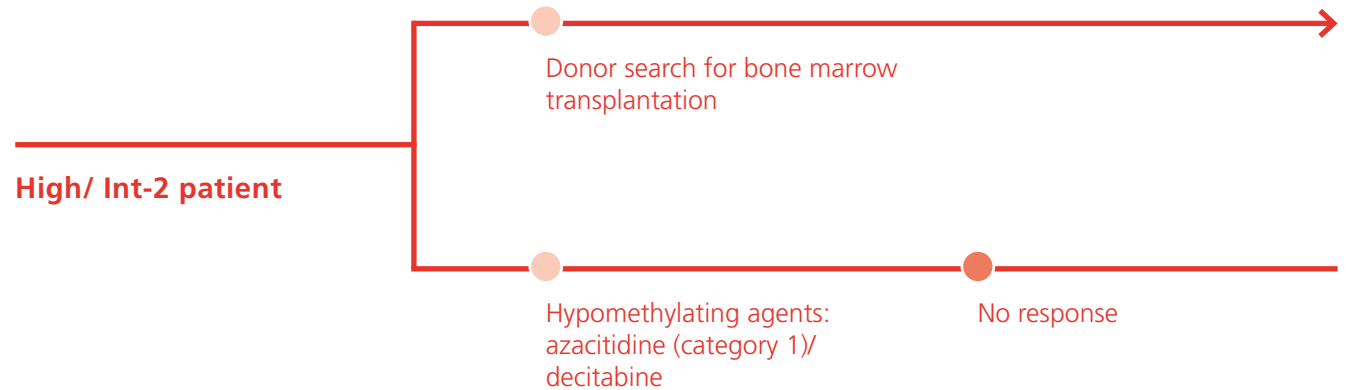


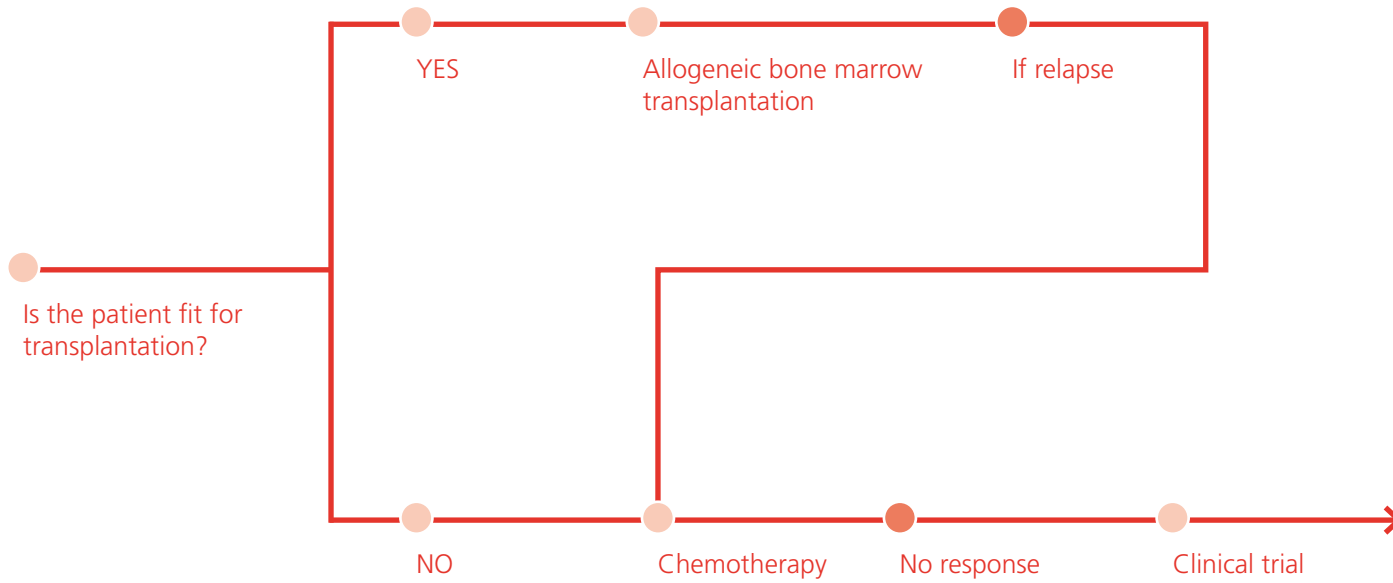




Myelodysplastic Syndromes

Potential MDS treatment algorithm: High-risk and Int-2







Multiple Myeloma

Diagnosis

Diagnosis requires at least:

- 1 major and 1 minor criteria, or
- 3 minor criteria (must include 1 and 2)
- Symptomatic patients with progressive disease

Major criteria

1. Plasmacytoma on biopsy
2. Marrow plasmacytosis > 30%
3. M-component:
Serum: IgG >3.5 g/dL;
IgA >2 g/dL
Urine: >1 gram light chain per 24 hours

Minor criteria:

1. Marrow plasmacytosis 10-30%
2. M-component present but less than above
3. Lytic bone lesions
4. Reduced normal immunoglobulins (<50% of normal)

Staging

Durie-Salmon Staging Criteria

Stage I

- All of the following:
1. Hemoglobin > 10g/dl
 2. Normal serum calcium
 3. On radiograph, normal bone structure or solitary bone plasmacytoma
 4. Low M-component production rates:
 - A. IgG < 5g/dl
 - B. IgA < 3g/dl
 - C. Urine light chain M-component on electrophoresis < 4g/24h

Stage II

Neither stage I nor stage III

Stage III

- One or more of the following:
1. Hemoglobin <8.5 g/dl
 2. Serum calcium >12mg/dl
 3. Advanced lytic bone lesions
 4. High M component production rates:
 - A. IgG > 7g/dl
 - B. IgA > 5g/dl
 - C. Urine light chain M-component on electrophoresis > 12g /24h

A= Creatinine < 2.0 mg / dl

B= Creatinine ≥ 2.0 mg / dl

Stage	Criteria	Median Survival (months)
I	Beta-2-microglobulin <3.5 mg/L and albumin ≥3.5 g/dL	62
II	Beta-2-microglobulin <3.5 mg/L and albumin <3.5 g/dL or beta-2-microglobulin 3.5 mg/L to <5.5 mg/L	44
III	Beta-2-microglobulin ≥5.5 mg/L	29

Prognosis

Risk Group	Cytogenetic Findings	Disease Characteristics
Standard risk	<ol style="list-style-type: none"> no adverse FISH* or cytogenetics, hyperdiploidy, t(11;14) by FISH*, or t(6;14) by FISH* 	These patients most often have <ol style="list-style-type: none"> disease that expresses IgG kappa monoclonal gammopathies and lytic bone lesions
High risk	Has any of the following cytogenetic findings: <ol style="list-style-type: none"> del 17p by FISH*, t(4;14) by FISH*, t(14;16) by FISH*, cytogenetic del 13, or hypodiploidy 	These patients have <ol style="list-style-type: none"> disease that expresses IgA lambda monoclonal gammopathies (often) and skeletal-related complications (less often)

*FISH = fluorescence *in situ* hybridization



Multiple Myeloma

Treatment



Isolated Plasmacytoma of The Bone

Radiation therapy to the lesion.

Chemotherapy, only in the setting of an increase of the M-spike with associated pertinent symptomatology. Options will be discussed in the section pertinent to symptomatic multiple myeloma below*.



Extramedullary plasmacytoma

Radiation therapy to the isolated lesion with planned radiation fields that cover the regional lymph nodes, if applicable.

Surgical resection may be considered in selected cases, but it is generally followed by radiation therapy.

Chemotherapy is required in the presence of disease progression with associated symptoms. Options will be discussed in the section pertinent to symptomatic multiple myeloma below.



Symptomatic Multiple Myeloma*

First line therapy

Young patients**
Age < 65-70

Thalidomide + Dexamethasone
Bortezomib + Dexamethasone

Older patients
Age > 65-70

Melphalan + Prednisone + Thalidomide
Melphalan + Prednisone + Bortezomib

Relapse or Progression

Previously mentioned treatments
Bortezomib + Liposomal Doxorubicin
If young, HDCT and autologous stem cell transplantation



Consolidation therapy

HDCT: autologous bone marrow or Cyclophosphamide and/or G-CSF mobilized peripheral stem cell transplantation.

- a. Regimen commonly used for HDCT:
Melphalan 200 mg/m². Adjusted doses of melphalan in certain situation is permissible.
- b. Strong evidence to support maintenance therapy with lenalidomide post autologous HCT.
(Risks of secondary malignancies have been reported)



Supportive therapies for all patients regardless of age

Bisphosphonates

DVT prevention

Anti-herpes therapy while prescribing bortezomib

*Available agents:

1. Steroids (prednisone, dexamethasone), 2. Immunomodulatory agents: Thalidomide, Lenalidomide, 3. Proteasome inhibitors: Bortezomib, 4. Conventional chemotherapy: Alkylators (Melphalan, Cyclophosphamide), Anthracyclines (Doxorubicin, Liposomal doxorubicin) and Vinca alkaloids (Vincristine).

**Candidates for autologous stem cell transplantation

08 Neuroendocrine Tumors

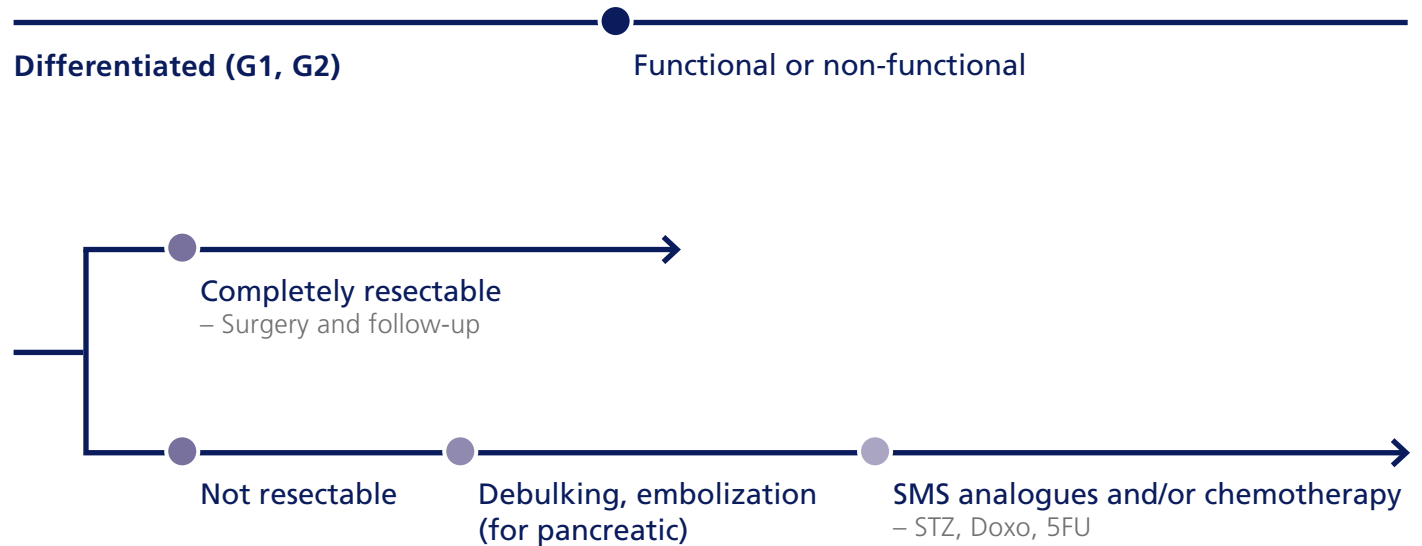


NET, bronchial, thymic or
gastroenteropancreatic tumors

08 Neuroendocrine Tumors



NET, bronchial, thymic or gastroenteropancreatic tumors





09 Adult Brain Tumors



Low grade astrocytoma

Recurrent low grade astrocytoma

Low grade oligodendroglioma,
or mixed oligoastrocytoma

Recurrent low grade oligodendroglioma,
or mixed oligoastrocytoma

Anaplastic astrocytoma

Recurrent anaplastic astrocytoma

Anaplastic oligodendroglioma,
or mixed oligoastrocytoma

Recurrent anaplastic oligodendroglioma,
or mixed oligoastrocytoma

Glioblastoma

Recurrent glioblastoma
(rule out pseudoprogression)

Low and high grade
intracranial ependymoma

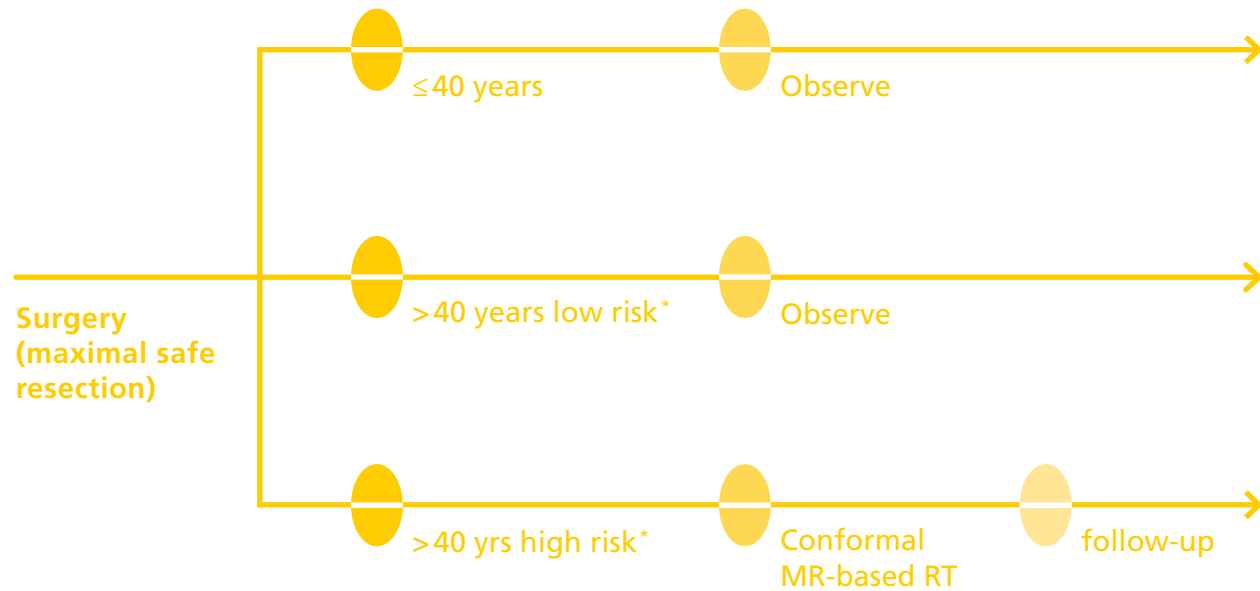
Recurrent low and high grade
intracranial ependymoma

Medulloblastoma and Supratentorial PNET

Primary CNS lymphoma: consider guidelines

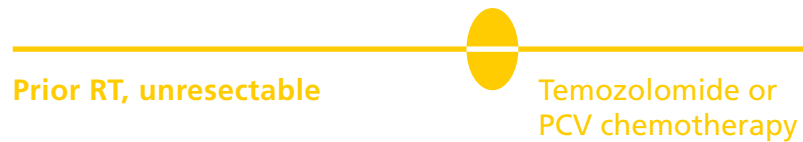


Low Grade Astrocytoma



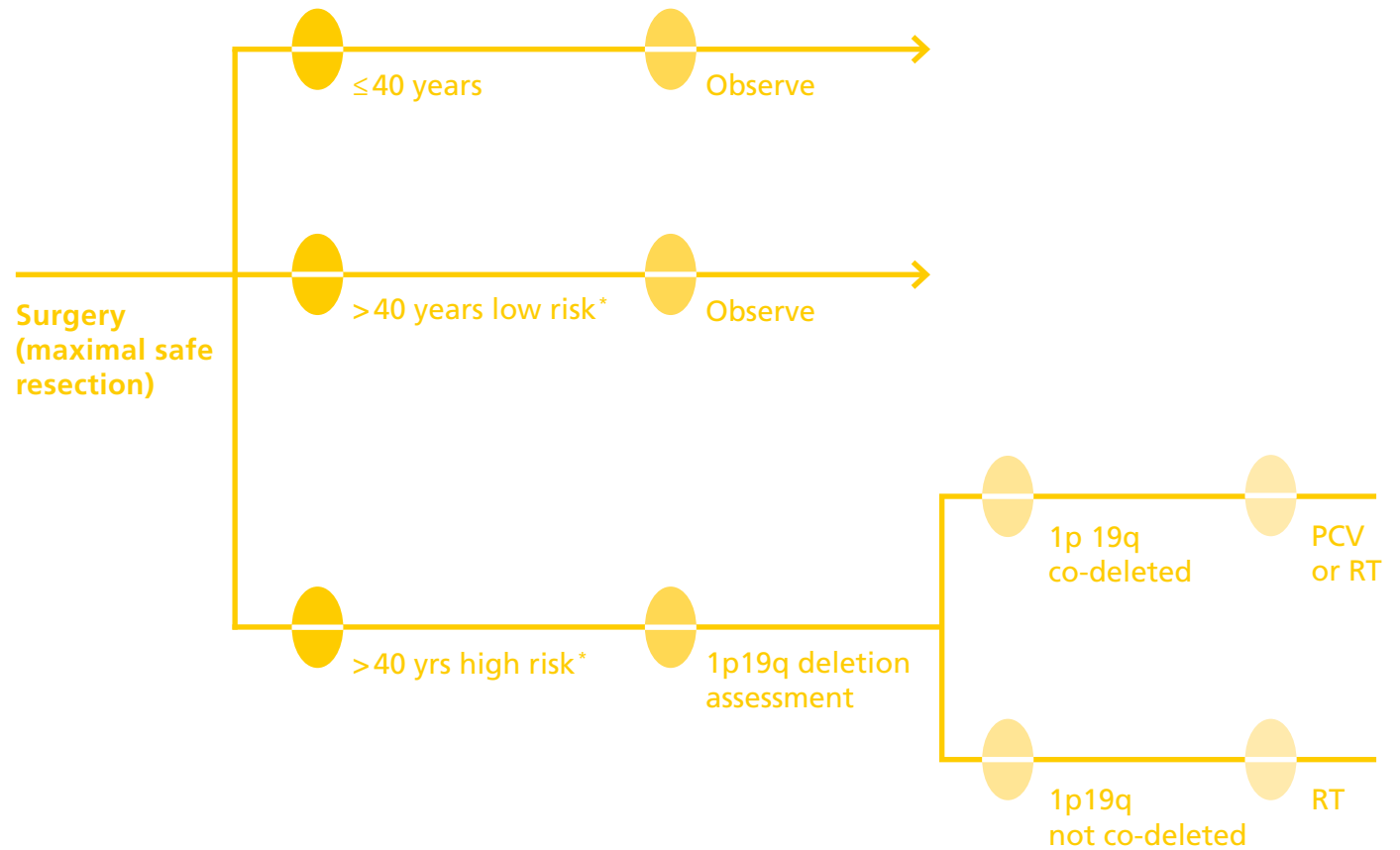
* Risk factors are age >40 years, astrocytoma histology, largest dimension >6 cm, tumor crossing midline, and presence of neurologic deficit. High risk patients are considered those with 2 or more of these factors.

Recurrent Low Grade Astrocytoma



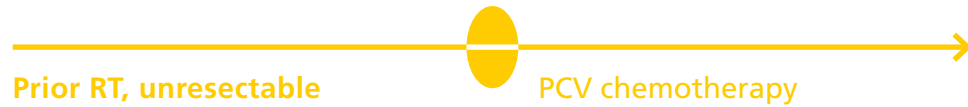
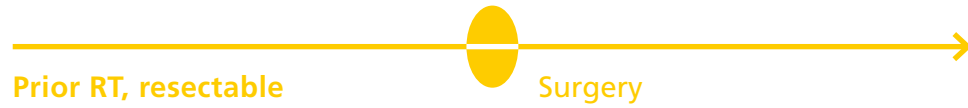


Low Grade Oligodendroglioma, or Mixed Oligoastrocytoma



* Risk factors are age > 40 years, astrocytoma histology, largest dimension > 6 cm, tumor crossing midline, and presence of neurologic deficit. High risk patients are considered those with 2 or more of these factors.

Recurrent Low Grade Oligodendroglioma, or Mixed Oligoastrocytoma





Anaplastic Astrocytoma



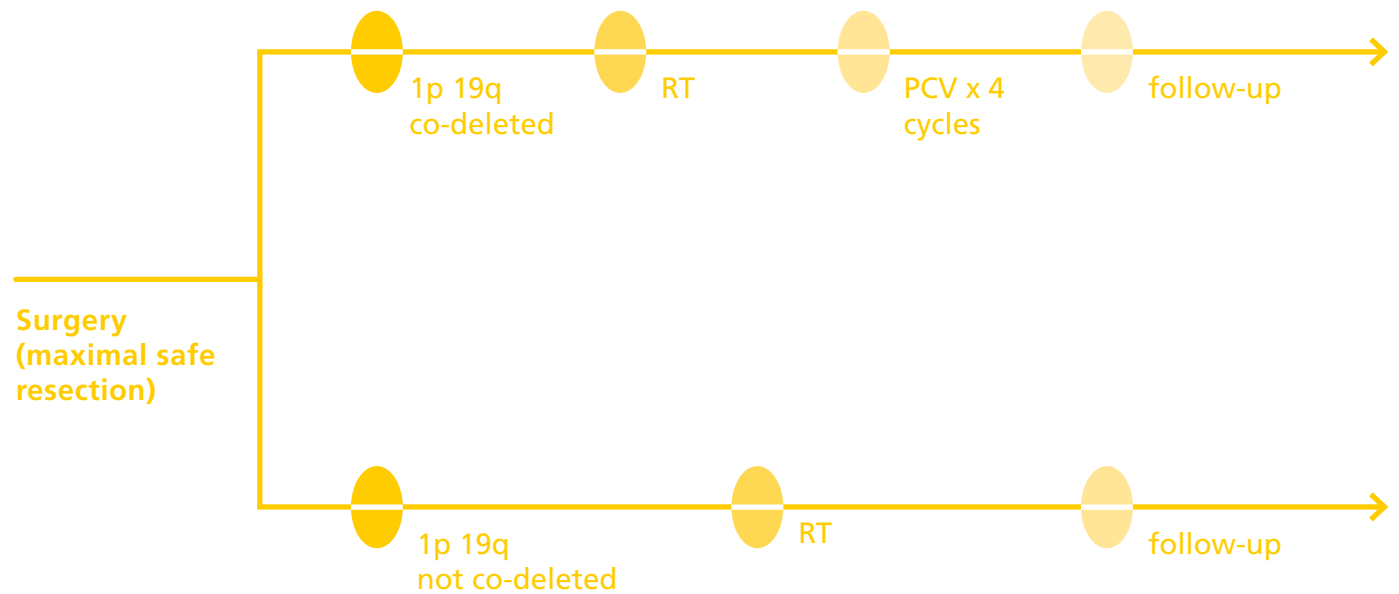
Recurrent Anaplastic Astrocytoma



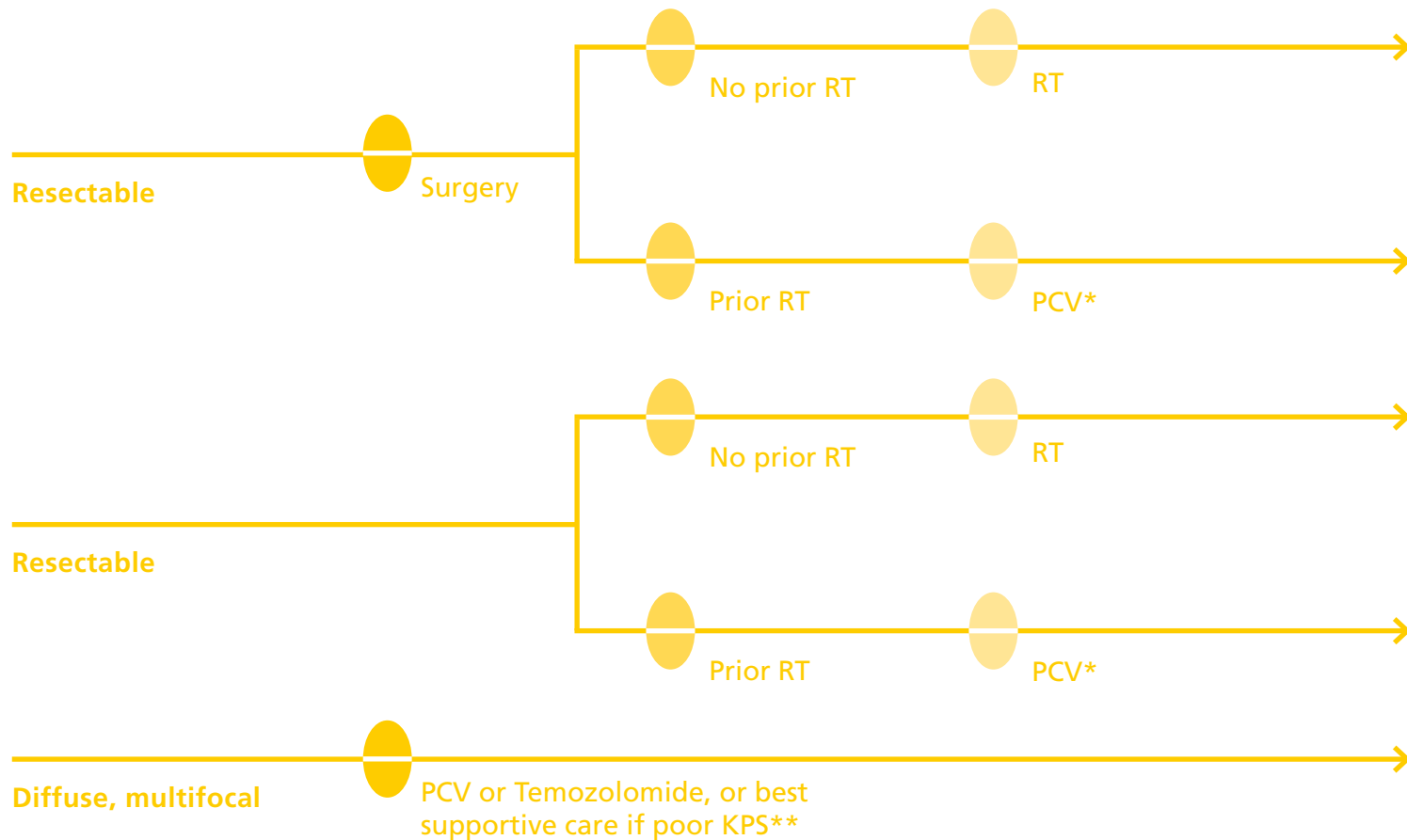
* Consider stereotactic re-irradiation



Anaplastic Oligodendroglioma, or Mixed Oligoastrocytoma



Recurrent Anaplastic Oligodendroglioma, or Mixed Oligoastrocytoma

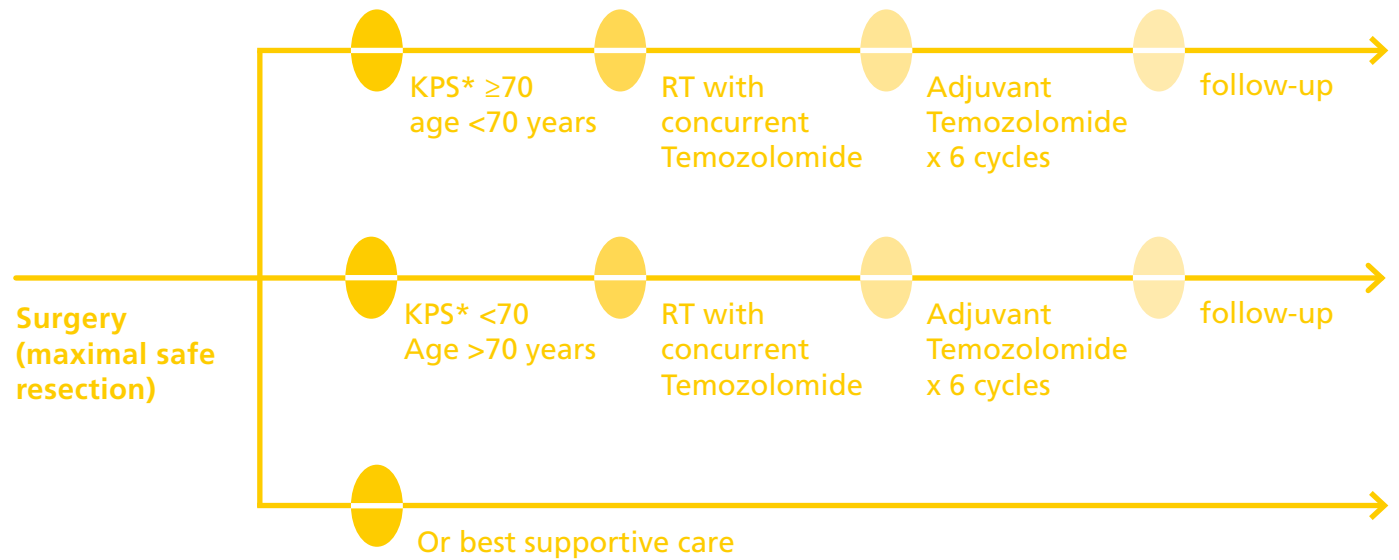


* Consider stereotactic re-irradiation

** KPS: Karnofsky Performance Score

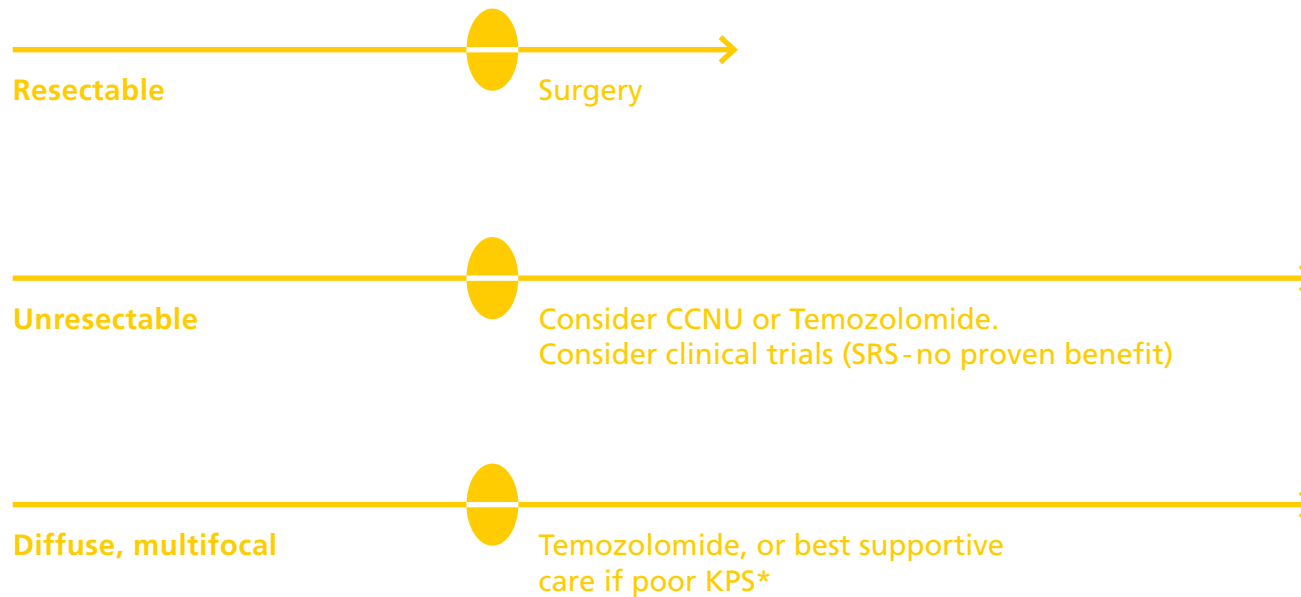


Glioblastoma



* KPS: Karnofsky Performance Score

Recurrent Glioblastoma (Rule Out Pseudoprogression)



* KPS: Karnofsky Performance Score



Low and High Grade Intracranial Ependymoma



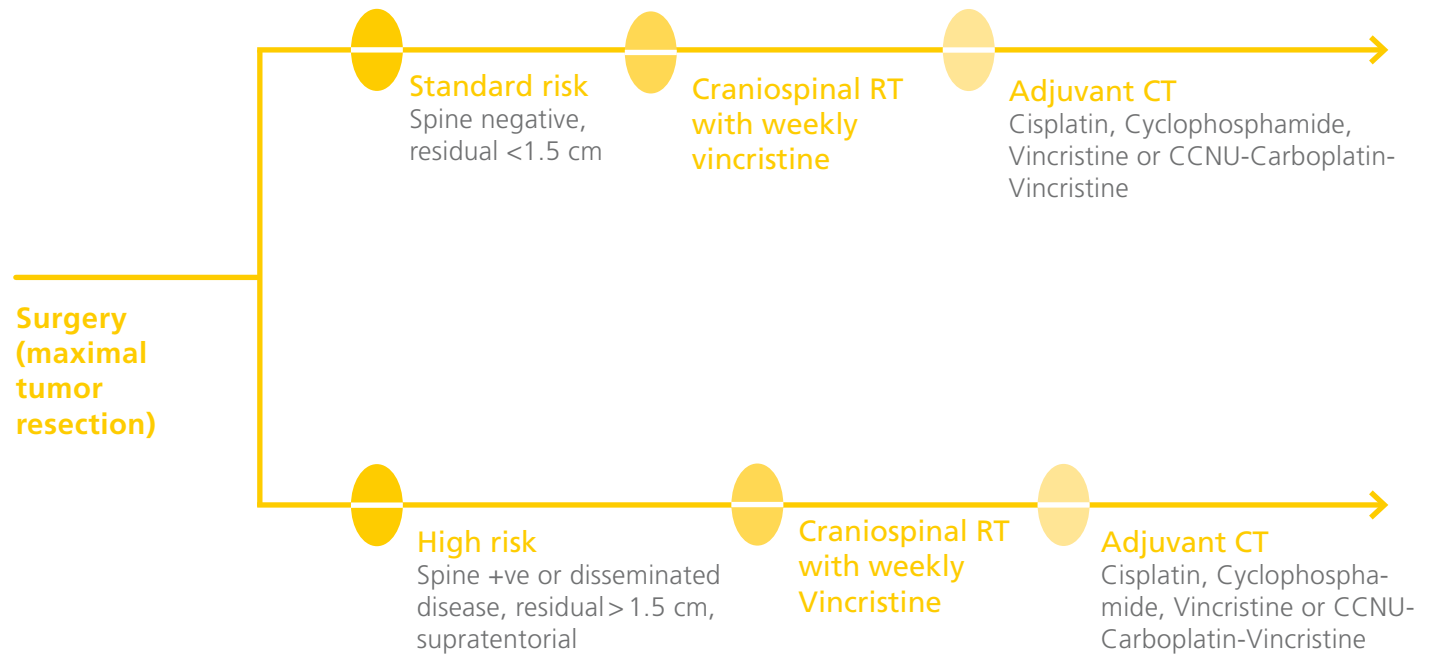
Recurrent Low and High Grade Intracranial Ependymoma



* Consider stereotactic re-irradiation



Medulloblastoma and Supratentorial PNET



Primary CNS Lymphoma

→ Consider guidelines



هذا المنشور هو ملحق رسمي تابع لقرار وزاري ١/٤٥٥ اصدره وزير الصحة الدكتور علي حسن خليل بتاريخ ٢١ نيسان ٢٠١١.

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عضو

الدكتور علي طاهر
عضو

الدكتور زياد سالم
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