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. Nizar Bitar	Oncology specialist

اللجنة العلمية لدراسة طلبات أدوية السرطان

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

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

لائحة بمراكز توزيع الأدوية في جميع المناطق اللبنانية

المركز الرئيسي لتوزيع الأدوية في الكرنتينا
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

Date / /

Patient Information

NCR ID: _____ Karantina ID: _____

إسم المريض: _____ إسم الأب: _____ إسم الأم: _____ الشهرة عند الولادة: _____

شهرة الزوج: _____ الجنس: ☐ ذكر ☐ أنثى تاريخ الولادة:--/--/-- رقم السجل: _____

محل الولادة: _____ البلد: _____

المحافظة: _____ القضاء: _____ البلدة: _____

عنوان السكن الدائم: _____ البلد: _____

المحافظة: _____ القضاء: _____ البلدة: _____ هاتف: --/------

Tumor Registry Information

Primary Site (text): _____

ICD-10: C____•__ Laterality: ☐ Right ☐ Left ☐ Bilateral ☐ Not applicable ☐ Unspecified

Date of first diagnosis: / / ICD-10 M __ __ __ __ / __

Pathology (text): _____

Classification: TNM(2) ☐ T ☐ N ☐ M Stage(3): Grade: Other Staging:

Pathology Center: _____ Pathologist: _____

Type of report: ☐ New case ☐ Known case

If Known Case
- ☐ Relapse
- ☐ Progression
- ☐ Change of treatment

If Relapse
- ☐ Local
- ☐ Regional
- ☐ Distal

Treatment

Finality of treatment: ☐ Palliative only ☐ Other

Prior Chemotherapy treatment: ☐ No ☐ Yes(4) Specify: _____

Type of treatment planned:

Surgery:	☐ No	☐ Yes
Chemotherapy(5):	☐ No	☐ Yes
No Radiotherapy:	☐ No	☐ Yes
Targeted therapy:	☐ No	☐ Yes
Immunotherapy:	☐ No	☐ Yes
Hormone therapy:	☐ No	☐ Yes

Physician Information

Physician Name: _____ Specialty: _____

LOP Registration No.: _____ Telephone: _____

Date: _____

Signature & Stamp: _____

Documents to be submitted for Antineoplastic drugs:

1 صورة عن إخراج قيد حديث لا يتعدى الشهر
2 Physician's prescription (Dosage & Schedule)
3 Detailed Medical Report
4 Pathology Report (Solid Tumor)
5 Laboratory Report (Blood Tumor)

N.B:
1 This form must be totally completed by the Doctor.
2 All Documents should be attached.
3 All attached reports and studies should be original and official.
4 Written enquiries are only accepted:
Attached to the medical file or by e-mail: drugs@public-health.gov.lb

(1) For reporting to NCR, form is sent 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.

Aknowledgements

Based upon the request of the ministry of health the **TOKTEN** project developed a project to support the ministry in its initiative to provide international standards of care for cancer patients subsidized by the Ministry of Health. A national committee was created by ministerial decision that includes 6 prominent Lebanese oncologists from different background in addition to the **UNDP TOKTEN** project manager *Mrs. Ariane Elmas*. The committee established guidelines that were then reviewed by expatriate doctors from distinguished international cancer centers. The project also received the financial support for the booklet and the launching event from a Lebanese Expatriate, *Mr. Monzer Hourani*.

I would like to acknowledge the contributions of the following groups and individuals to the successful completion of this project:

It is an honor to have worked with *Minister Dr. Mohamad Jawad Khalifeh and his team*. We are thankful for their vision and relentless commitment in the aim of providing international standard of care for cancer patients covered by the Ministry of Health.
The distinguished oncologists of the national and international committee volunteered their knowledge, expertise and time for the development of precise and comprehensive guidelines.

I would like to show my gratitude to our reviewers from international cancer centers namely *Dr. Ahmad Awada, Dr. Fadlo Khoury, Dr. Anthony El-Khoueiry, Dr. Maurie Markman Dr. Nizar Tannir Dr. Lajos Pusztai and Dr. Anas Younnes.*

We owe our deepest gratitude to the coordinator of international committee and reviewer *Dr. Jean Pierre Issa*.

These guidelines would not have been possible without the persistence and dedication, in elaborating evidence based protocols, of the national committee. Accordingly we would like to profoundly thank *Dr. Fadia Elias, Dr. Joseph Kattan, Dr. Ghazi Nsouli, Dr. Ziad Salem, Dr. Ali Shamseddin* and in particular the head of the committee *Dr. Nizar Bitar* for his continuous proactive leadership.
I am grateful for the advisory support provided to the national committee by *Dr. Muhieddine Seoud, Dr. Ali Bazerbachi and Dr. Ahmad Ibrahim.*

Dr. Wassim Wazzan has made available his support in a number of ways since the inception of this project. I would like to show my appreciation for *Mr. Monzer Hourani* for believing in this project and supporting it.

It is a pleasure to thank those who made this booklet a user-friendly guide. Editorial assistance was provided by *Manuscript Experts S.A.R.L.*and graphic design by *KITE, a branding concept by Koein"*.
Lastly, I offer my regards and blessings to all of those who supported this initiative in any respect during the completion of the project.

Marta Ruedas,
UNDP Resident Representative

كلمة معالي وزير الصحة العامة
الدكتور محمد جواد خليفة

الأمراض المستعصية ليست فقط أمراض بالغة الخطورة ومزمنة وصعبة العلاج بل إن توفر العلاج وتوقيته مرتبط ارتباطاً مباشراً باستمرارية الحياة ونوعيتها وأن أي خلل قد يؤدي إلى الوفاة أو تدهور صحة الانسان. يضاف إلى ذلك أن كلفة العلاج من دواء واستشفاء وحاجات خاصة ليست بمقدور معظم المواطنين حتى يذهب البعض في تسمية هذه الأمراض بـ Catastrophic Illness. والأمراض السرطانية على أنواعها تقع ضمن هذا التعريف.

ففي لبنان هناك تزايد لاعداد مرضى السرطان , حيث ان هناك 8000 حالة سرطانية جديدة تسجل سنويا (بناءا للسجل الوطني للسرطان).

و على هذا الصعيد, يحصل المريض الذي لا يوجد لديه أي تغطية صحية على الدواء من وزارة الصحة العامة بتغطية نسبتها 100% اي ان هناك أكثر من 50% من مرضى السرطان في لبنان يحصلون على أدويتهم من وزارة الصحة العامة مجاناً دون دفع أي فروقات . و تشكل كلفة علاج مرضى السرطان في وزارة الصحة العامة 53 % من مجمل كلفة أدوية الأمراض المستعصية.

و يتم استلام الادوية من خلال مركز توزيع الادوية المركزي في الكرنتينا بالاضافة الى 5 مراكز تم استحداثها في جميع المناطق اللبنانية لتسهيل العملية على المواطنين في كل من: مستشفى صيدا الحكومي, مستشفى طرابلس الحكومي, مستشفى زحلة الحكومي, مستشفى النبطية الحكومي, مستشفى بيت الدين الحكومي.

ولقد بدأ العمل بهذه المراكز بعد أن تم تجهيزها بالمعدات اللازمة لزوم فرش مكتبي، ونظام معلوماتية، وبرادات لتخزين الأدوية وحفظها وبالتعاون مع منظمة الصحة العالمية ، إضافة إلى أن رئيس كل مركز هو مفتش صيدلي يقوم باستلام الطلبات من المرضى وإرسالها إلى اللجنة العلمية في بيروت، و استلام الدواء من المستودع المركزي وتسليمه إلى المواطن دون حاجة المواطنين للسفر من المحافظات إلى بيروت. و المراكز مربوطة الكترونياً بالمستودعات المركزية بشكل واضح بحيث لا يمكن المواطن من استلام الدواء من أكثر من مركز.

اما بما يتعلق باللجنة العلمية, فتقوم هذه اللجنة بدراسة طلبات ادوية السرطان مرتين أسبوعياً حيث يتم التاكد من المستندات المقدمة والموافقة على الدواء الموصوف إذا كان من ضمن بروتوكولات العلاج المتبعة، وتحديد الفترة الزمنية للعلاج وتتابع اللجنة مع المريض أي خلل في الوصفة الطبية. كما تقوم اللجنة بدراسة جدوى تمديد فترة العلاج لفترة زمنية جديدة بناء لاقتراح الطبيب إذا اقتضى الأمر بعد انتهاء مدة العلاج المقترحة سابقا.

و لتفعيل عمل هذه اللجنة بهدف ترشيد استخدام الدواء والموارد المتاحة مما لا يتعارض مع مصلحة المريض و ينعكس ايجابا على كلفة علاجه,
و نظرا لأهمية وضع ضوابط لكيفية وصف أدوية المراض السرطانية للمرضى المستفيدين من تقديمات وزارة الصحة العامة, قامت وزارة الصحة بتشكيل لجنة وطنية لوضع بروتوكولات علاجية بناء على لائحة الادوية المعتمدة في وزارة الصحة و ذلك بالتعاون مع اخصائيين من لبنان و الخارج (بمن فيهم خبراء من المركز الطبي الأمريكي MD Anderson), فوضعت اللجنة و بناء على براهين علمية عالمية مجموعة بروتوكولات علاجية ذات مقاييس علمية.
إن اعتماد هذه البروتوكولات هو أسوة بالدول المتقدمة والغنية التي تحدد نوع العلاج المقدم من قبل الدولة وذلك ليس بهدف ترشيد الإنفاق المادي فقط، بقدر ما هو لتقديم أفضل أساليب العلاج المجدي للمريض والتي يستند على أدلة وبراهين تثبت سلامة الدواء المستعمل وقدرته على السيطرة على المرض وعلاجه في كثير من الأحيان.وهناك أمثلة عديدة عن أدوية باهظة الثمن أثبت علمياً عدم جدواها.

وان هذا الكتيب القيم و الدقيق الذي اعد بناء على الصيغة النهائية للبروتوكولات بعد الأخذ بعين الأعتبار رأي و ملاحظات جميع الجمعيات العلمية المعنية و نقابة الأطباء من شأنه أن يتيح السبيل للأطباء, و يسهل عليهم الأطلاع على بروتوكولات علاج الامراض السرطانية المعتمدة من قبل وزارة الصحة, التي ستعمل جاهدة على تأمين هذه الأدوية بصورة مستمرة للمواطنين المستفيدين من تقديمات وزارة الصحة. وبناءً على المتغيرات العلمية سيتم مراجعة هذا الكتيب كلما دعت الحاجة.

نشكر كل الذين عملوا على اصدار هذا الكتيب, و ننوه بجهود جميع الأطباء الذين شاركوا في وضع هذه البروتوكولات, و تقدير خاص الى الدعم المقدم من TOKTEN Project (UNDP/CDR).

وزير الصحة العامة
د. محمد جواد خليفة

Introductory Notes

On behalf of the team of external reviewers, we would like to express our thanks for allowing us to be involved in this remarkable project. Oncology today is at a crossroads. Advances are coming in fast and furious, extending lives and providing hope for patients and their families. These past few years, each major meeting has seen promising new drugs or new uses for existing drugs that can be rapidly implemented in the clinic. This explosion of information presents a difficult burden for clinical oncologists. We are called upon to implement advances rapidly and in a cost-effective way, and it has been difficult to strike the right balance between under-treatment that compromises survival and over-treatment that brings with it increased complications, hospitalizations, costs etc. Recognizing this problem, US oncologists turned several years ago to treatment guidelines prepared by disease-specific experts to help patient management.

Physicians are trained in the Art of Medicine and have long been reluctant to implement guidelines, believing strongly in the individualized nature of medical care. However, over the years, we have come to accept that personalized medicine is nothing more than finding the right guideline for the right patient. With the looming revolution in molecular medicine where each patient will be treated according to the biologic nature of their disease, guidelines become ever more important to ensure the utmost quality of care. Today, the optimal use of drugs such as trastuzumab in breast cancer, erlotinib in lung cancer, cetuximab in colon cancer and lenalidomide in MDS requires a thorough knowledge of tumor biology, tumor stage, and the natural history of the disease. In such situations, guidelines have emerged as the best way to treat the majority of affected patients in a clinically sound, consistent and accountable manner.

As a group, we feel that the development of country specific guidelines is absolutely required in oncology. Disease prevalence and even natural history can differ markedly between nations. The availability of treatments is also variable, and treatment choice is greatly influenced by local factors. The US has moved decisively towards outpatient chemotherapy while physicians and patients in some countries prefer inpatient chemotherapy. The availability of advanced care (e.g. stem cell transplantation), supportive care, palliative care and the ability to pay for new medications all differ substantially between countries. For these reasons, we applaud the efforts of the team of Lebanese oncologists who put together the treatment guidelines described in this book.

The process that led to these guidelines was generally similar to other guidelines put together by oncology societies or dedicated hospitals. A team of Lebanese specialists proposed treatment guidelines and these were peer-reviewed by a team of international oncology experts who provided input and suggestions in some cases. The final product should be viewed as a first step in what will be by necessity a dynamic process. Some relatively infrequent malignancies were not included. Others have very limited therapeutic options at present. For some cancers, treatment recommendations are bound to change in the next few months. Thus, a process was put in place to allow modifications of the guidelines, which will then be reviewed periodically. Moreover, the appropriateness of the treatment algorithms has to be tested in the real world, in the clinics of physicians who are actively prolonging the lives and relieving the suffering of patients with cancer.

It is our sincere hope that these guidelines will be helpful in achieving optimal cancer care in Lebanon.

Jean-Pierre Issa, MD
University of Texas MD Anderson Cancer Center, Houston, Texas

Fadlo Khuri, MD
Emory University, Atlanta Georgia

Introductory Notes

The global cancer burden is increasing. 10 million new cases per year were diagnosed in 2000; 16 million will be by 2020. Remarkably, 70% of these cases will be in the developing world, where the number will grow from 5.2 million annually to 8.8 million by 2020.

Development of new drugs is also rapidly growing. A new generation of anticancer drugs is emerging with different modes of action, toxicity profiles and efficacy. The major concern is their cost which has an important impact on their availability, accessibility and their proper use, efficacy versus effectiveness. Several hundred of such drugs are now under development in high income industrialized countries where the use of these very expensive drugs is recommended despite their marginal benefit. In our country a minority of people have access to these drugs. Their use has been made possible because of the sponsor of health authorities meaning the MOH.

The principal aim of this work is to propose the optimal treatment, evidence based, to the right patient at the right moment to achieve the optimal benefit using properly our limited resources.

I would like to thank H.E the Minister of Public Health Dr M.J. Khalifeh for this innovative initiative, Mrs. Ariane Elmas from the UNDP for her coordination and her assiduity, and all my colleagues without their commitment, this work would have never been achieved.

"Special thanks to Dr Wassim Wazzan RHUH CEO who was instrumental in initiating and supporting this project."

Dr. Nizar Bitar
Head of National Committee for Cancer Treatment
Sahel General Hospital
Lebanese university, Faculty of Medical Sciences
Hematology Oncology Head of Division
RHUH, member of the administrative Board

CONTENTS

01 Head And Neck

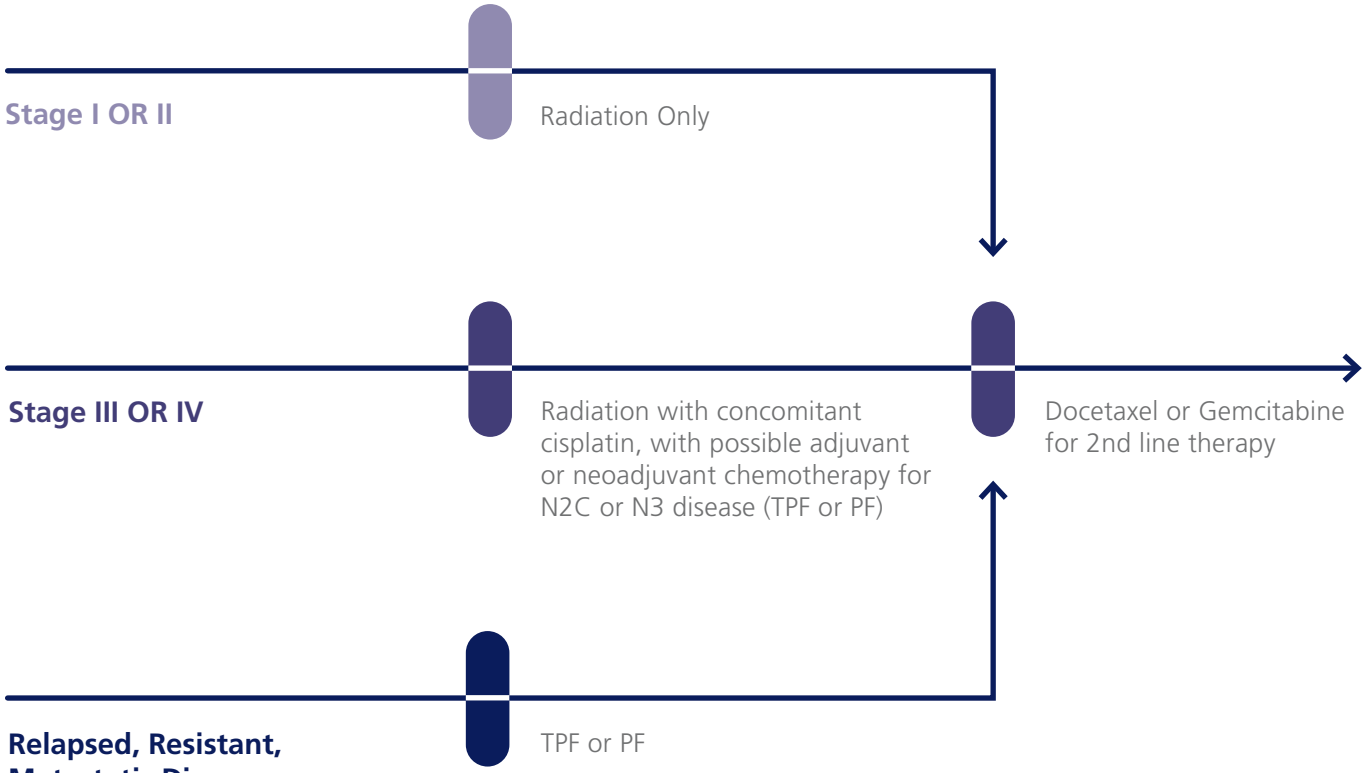
Nasopharynx

Squamous Cell Cancers of the Head and Neck

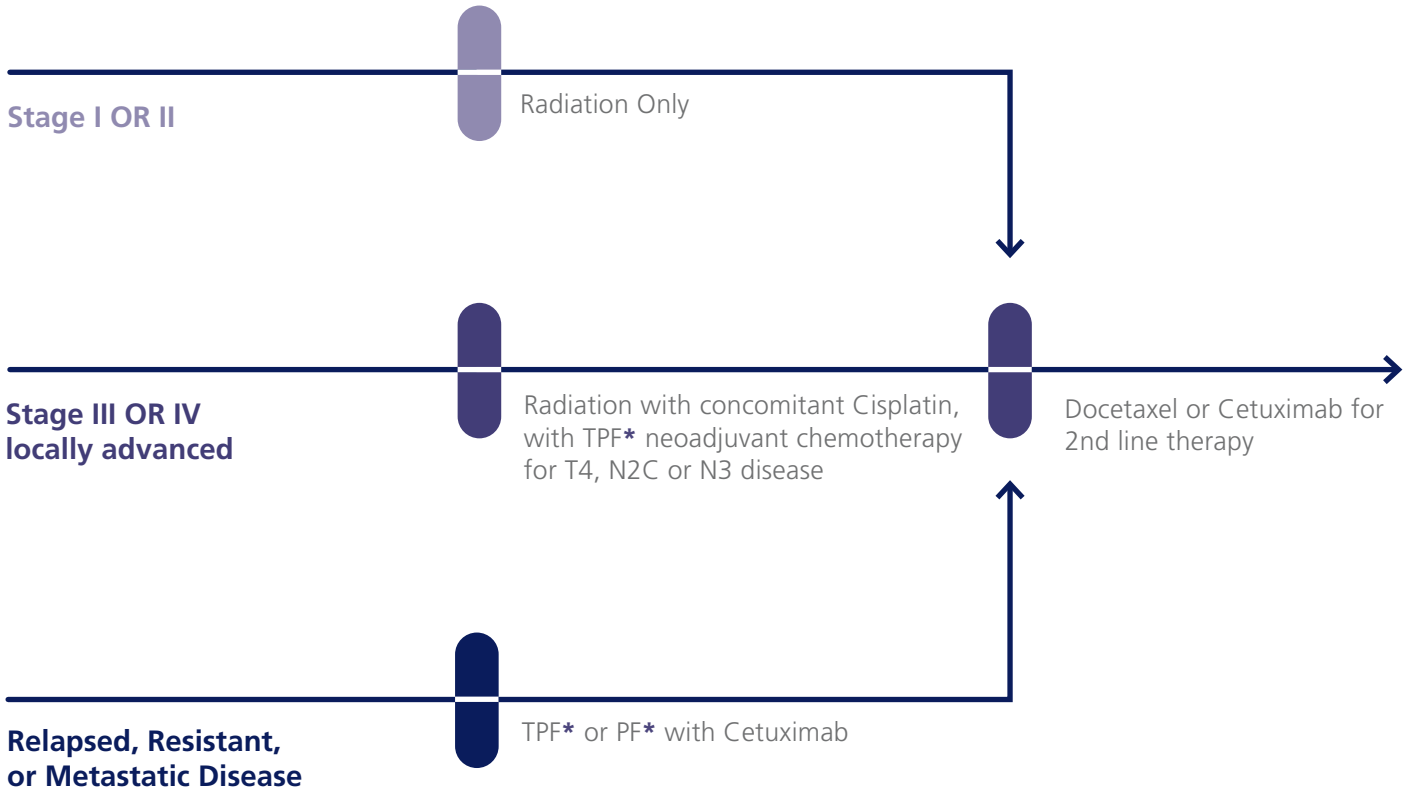
Oropharynx

Oral cavity

Nasopharynx

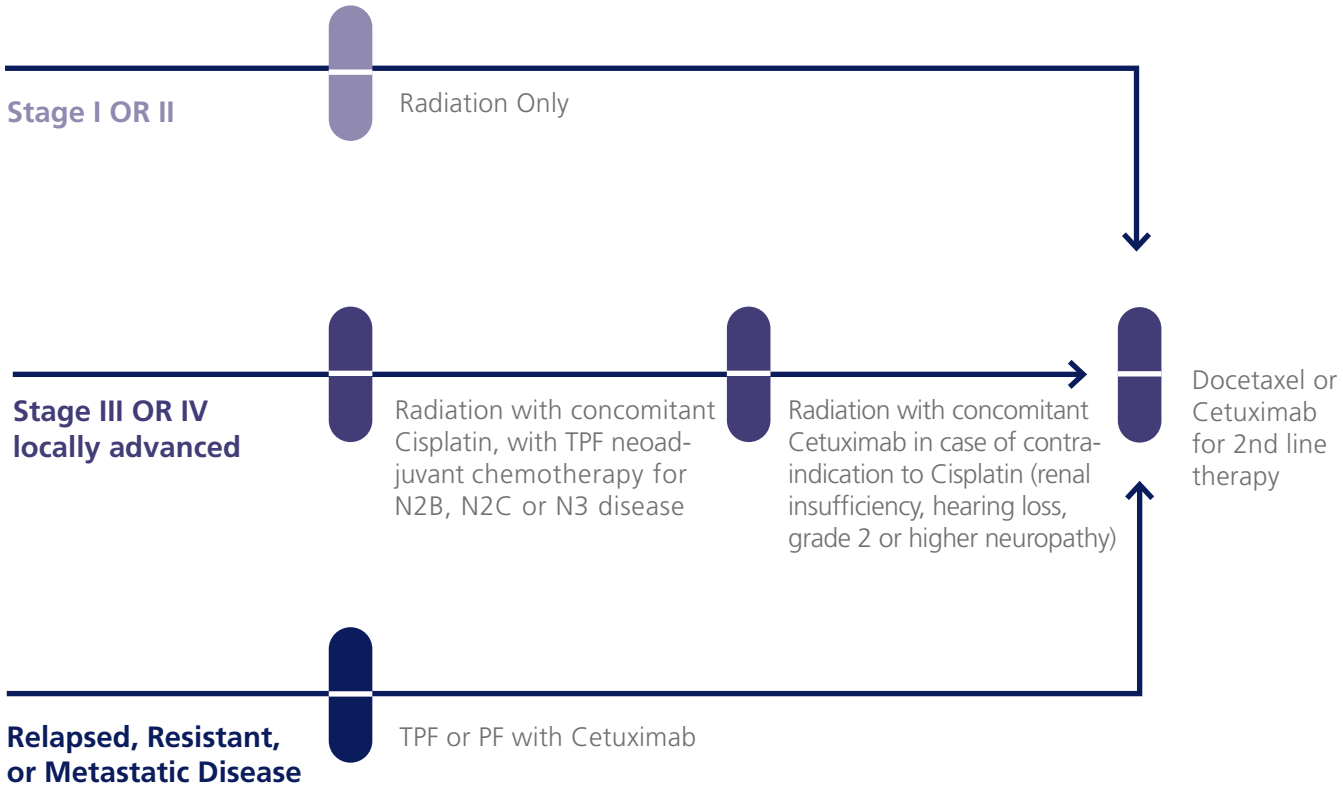


Squamous Cell Cancers of the Head and Neck, Larynx



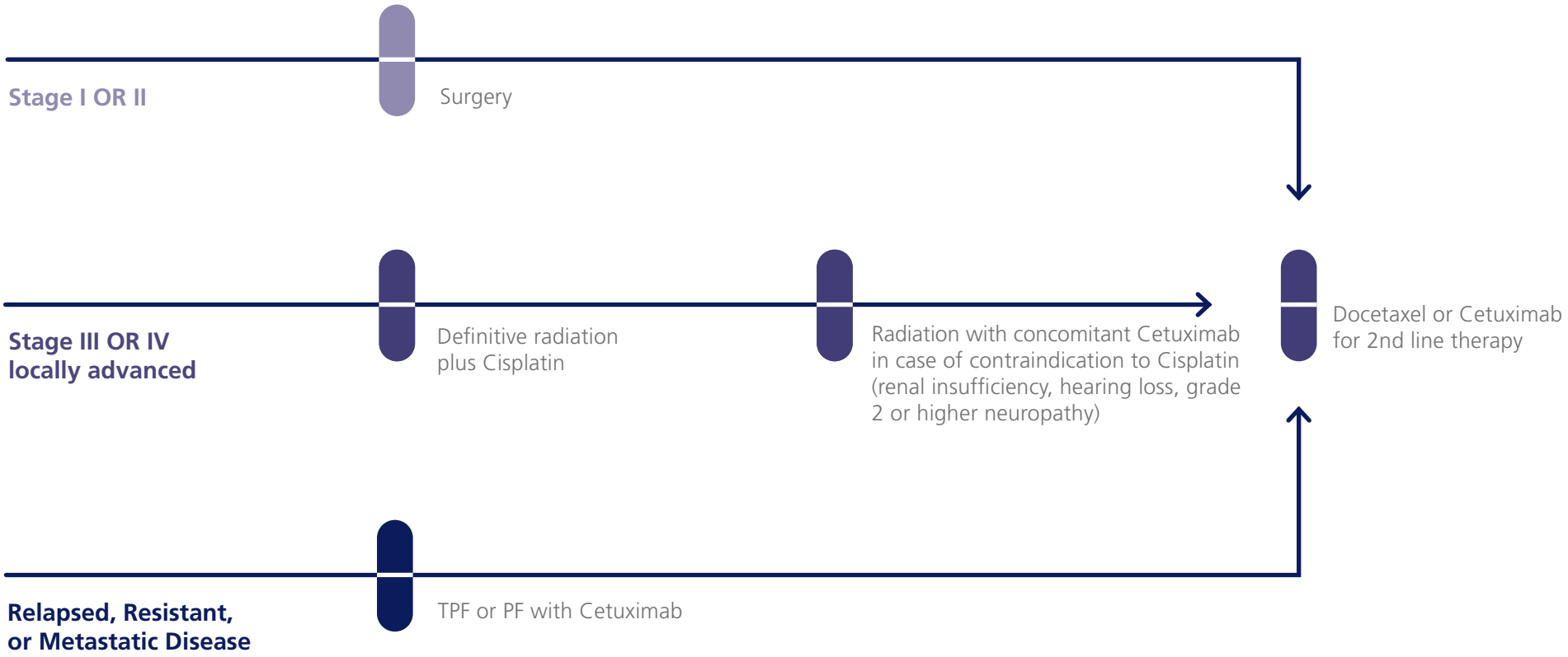
* TPF: Docetaxel, Cisplatin, 5-FU
PF: Cisplatin, 5-FU

Oropharynx



Consider testing for HPV

Oral Cavity


Stage I OR II
Surgery
Stage III OR IV
locally advanced
Definitive radiation
plus Cisplatin
Radiation with concomitant Cetuximab
in case of contraindication to Cisplatin
(renal insufficiency, hearing loss, grade
2 or higher neuropathy)
Docetaxel or Cetuximab
for 2nd line therapy
Relapsed, Resistant,
or Metastatic Disease
TPF or PF with Cetuximab

02 Lung Protocols

Small Cell Lung Cancer

Bronchoalveolar Carcinoma

Mesothelioma

Non small cell lung cancer
(except bronchoalveolar)

Small Cell Lung Cancer

Limited Disease

1st line
Etoposide+Platinum+RT
Whole brain radiation

2nd line sensitive relapse
Platinum
Irinotecan

Advanced Disease

1st line
Etoposide+Platinum
Consider whole brain radiation
Etoposide+Platinum/
VCA/irinotecan

2nd line sensitive relapse
Topotecan

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

First line

Platinum/Vinorelbine
Platinum/Docetaxel
Platinum/Gemcitabine

Adenocarcinoma
Cisplatin-Pemetrexed,
Gefinitib (non smoker
with EGFR mutation)

* Carboplatin if Cisplatin is contraindicated

Second line for stage IV

Docetaxel; Platinum-Vinorelbine
if sensitive relapse

Erlotinib

03 Breast Cancer

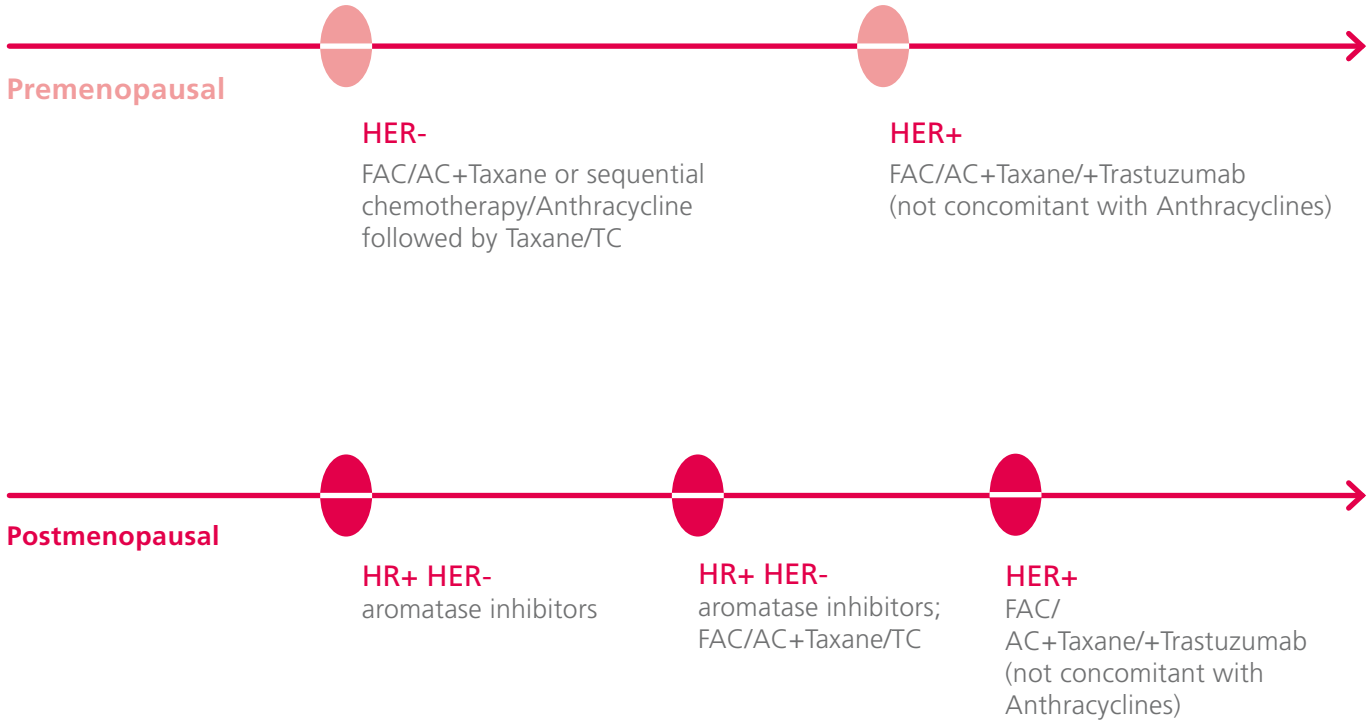
Neoadjuvant

Metastatic

Adjuvant therapy for HER-2/ neu positive tumors

Adjuvant therapy for HER-2/ neu negative tumors

Neoadjuvant



Premenopausal Metastatic Breast Cancer

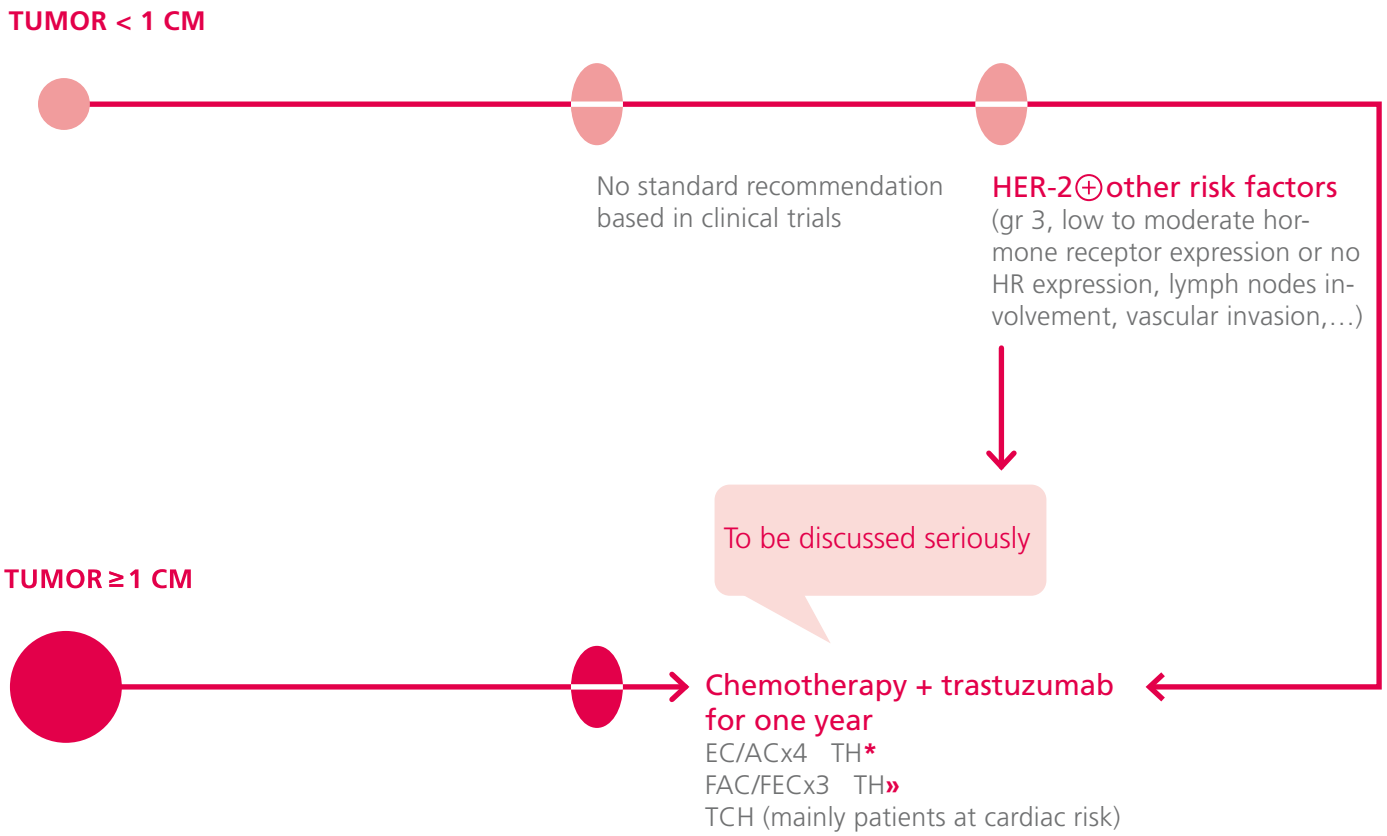
HR- HER-	HR- HER+	HR+ HER+	HR+ HER-	Non bulky or symptomatic disease	Bulky and/or symptomatic disease
FAC/AC/Taxane/ Taxane Gemcitabine/ Cisplatine Vinorelbine/ Vinorelbine Capecitabine/ Capecitabine/Docetaxel Capecitabine/CMF/ Liposomal Doxorubicin (restricted to decreased EF)	FAC/AC/taxane/ Taxane Gemcitabine/ Cisplatine 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/ Cisplatine Vinorelbine/ Vinorelbine Capecitabine/ Capecitabine/ Docetaxel Capecitabine	Tamoxifen, LH-RH agonist + tamoxifen, oophorectomy + tamoxifen, Aromatase inhibitors restricted to FSH/LH/Estradiol levels compatible with post-menopausal status*	FAC/AC/taxane/Taxane Gemcitabine/Cisplatine Vinorelbine/Vinorelbine Capecitabine/ Capecitabine/Docetaxel Capecitabine/CMF/Liposomal doxorubicin (restricted to EF bordeline) 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

Postmenopausal Metastatic Breast Cancer

HR- HER-	HR- HER+	HR+ HER+	HR+ HER-
FAC/AC/Taxane/Taxane Gemcitabine/Cisplatine Vinorelbine/ Vinorelbine Capecitabine/Capecitabine/ Docetaxel Capecitabine/ CMF/ Liposomal Doxorubicin (restricted to decreased EF)	FAC/AC/taxane/Taxane Gemcitabine/ Cisplatine 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 / aromatase inhibitor +/- trastuzumab	Tamoxifen, aromatase inhibitor (Letrozole, Anastrozole), in first and second line, Exemestane in third line after second line AI

Adjuvant Therapy for HER+



* (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 low risk (HR+ low to moderate expression) Grade 2
Negative lymph nodes
Moderate proliferation index (10-20%)

→ AC x 4
EC x 4
CMF x 6
TC x 4
FEC x 6
FAC x 6
Followed by Endocrine therapy*

Luminal B high risk and triple negative
(HR+,≥ gr2, high proliferative index) +/- positive lymph nodes +/- other risk factors (e.g., lympho-vascular invasion) or

→ FEC/FAC x 6
3 FEC → 3 Docetaxel
4 AC → 4 Docetaxel or weekly paclitaxel x 12
TC x 4 (in pts at cardiac risk)
FAC/FEC → CMF

* Endocrine therapy: - premenopausal: Tamoxifen
- postmenopausal: sequential treatment

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

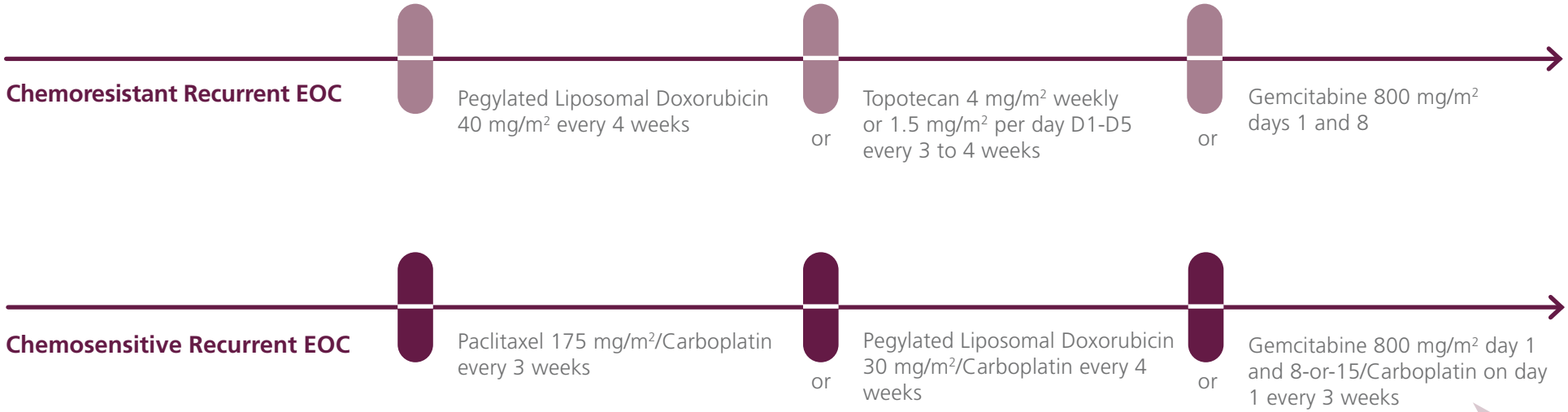
Advanced EOC

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 Cisplatinum 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

Early stage
concomitant chemoradiotherapy with cisplatin

Advanced Stage
platinum-based chemotherapy

05 Gastrointestinal

Colon Cancer

Rectal Cancer

Pancreatic Cancer

Biliary and Gallbladder Cancer

Esophageal Carcinoma

Hepatocellular Carcinoma

Small Intestine Carcinoma

Gastric Carcinoma and GE Junction

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 or Panitumumab)

→ 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 (Erbitux)

Rectal Cancer

Neoadjuvant
(For T3 or T4 or lymph node positive with any T)

→ Chemoradiation

5-FU based Capecitabine (continuous IV infusion 200mg/m^2/day) 800mg/m^2 Q 12 h. for 5 days every week with XRT **OR** Capecitabine 800mg/m^2 Q 12 h. for 5 days every week **OR** 900mg/m^2 for 5 days every week with XRT

→ Surgery → Adjuvant Chemotherapy

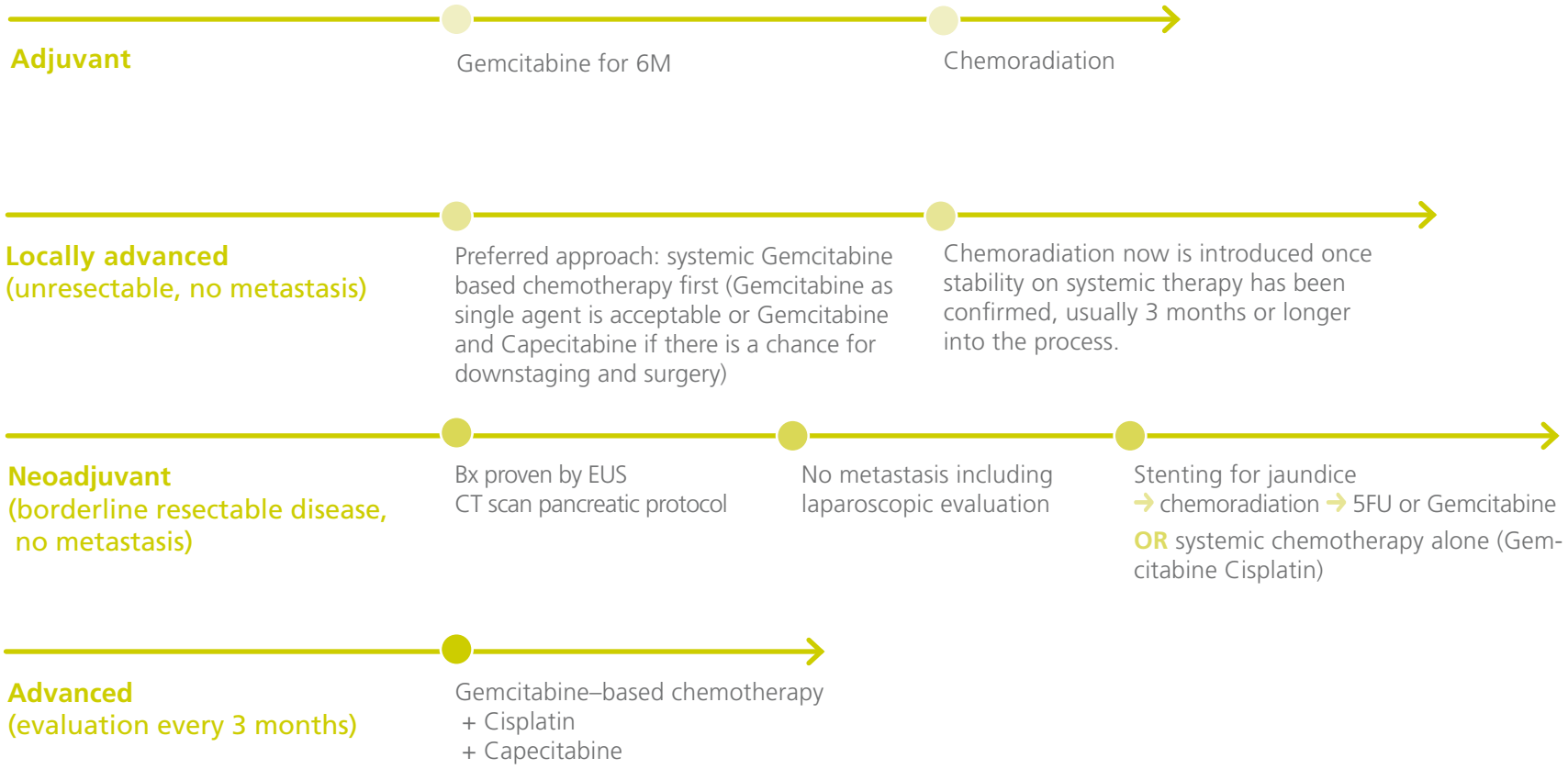
based on colon cancer guidelines

Adjuvant and advanced

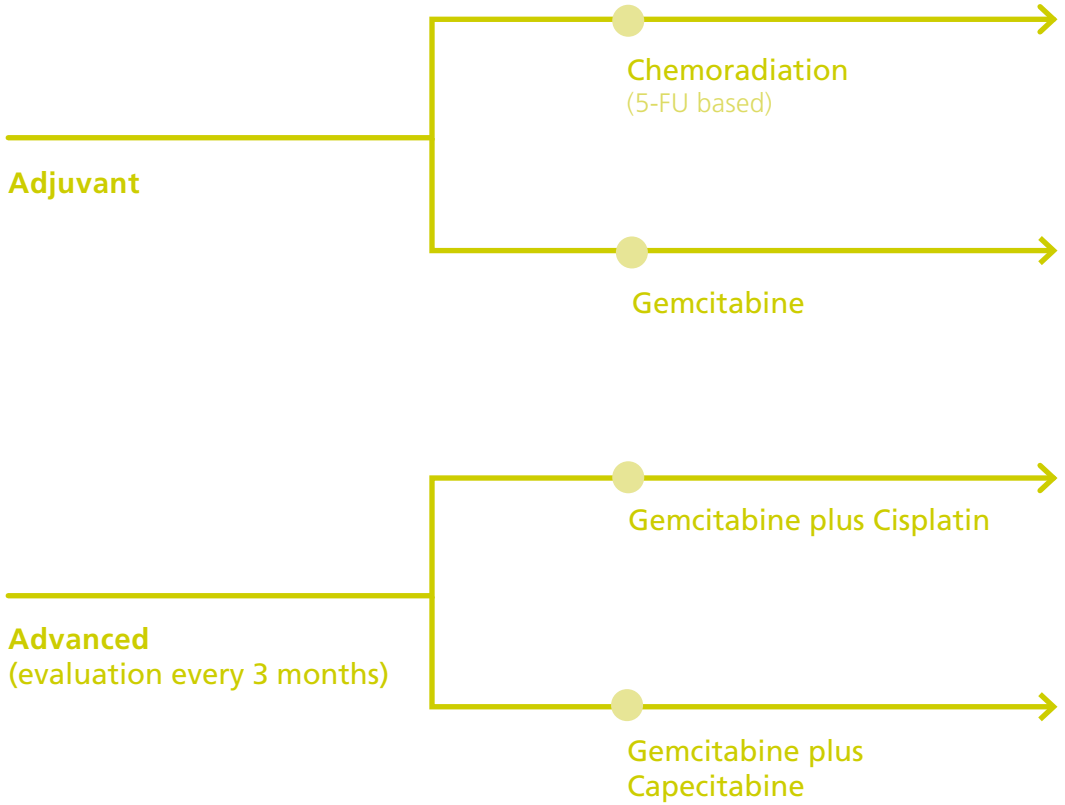
→ Treat as colon cancer

Evaluation every 2-3 months

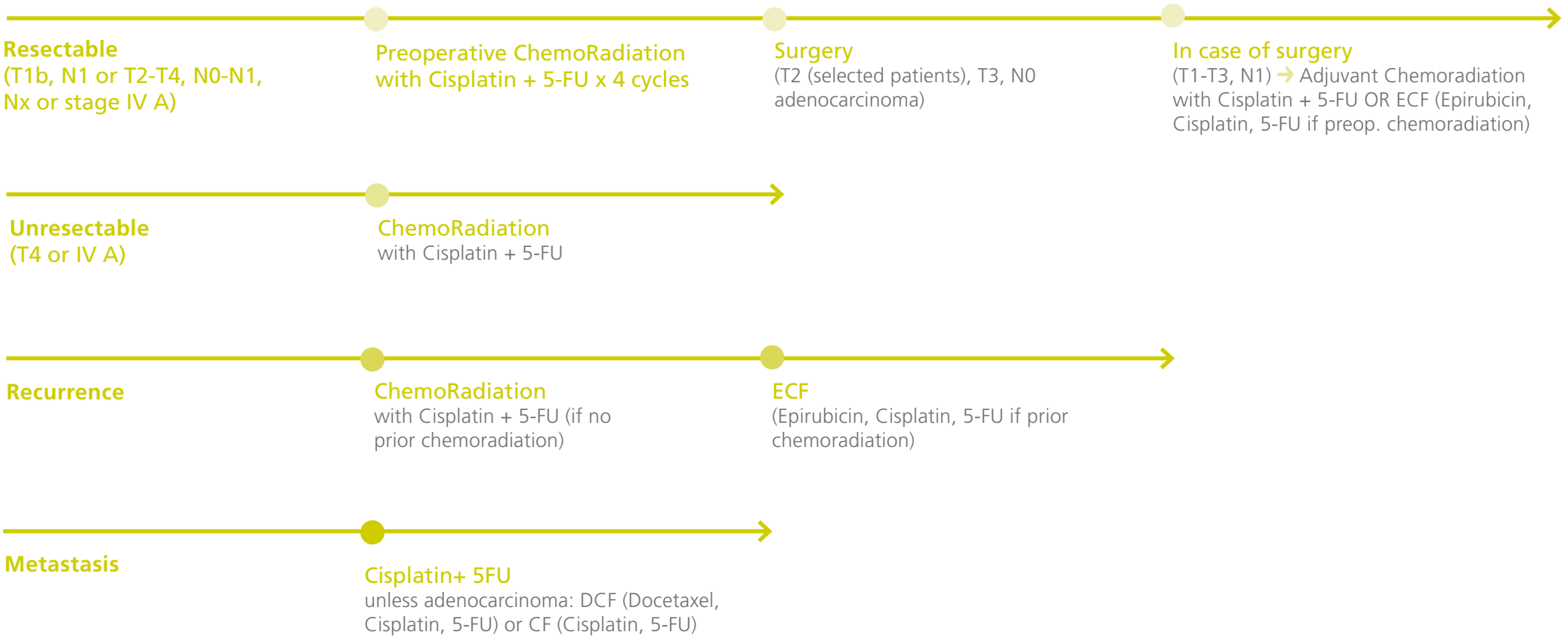
Pancreatic Cancer



Billiary and Gallbladder Cancer



Esophageal Carcinoma



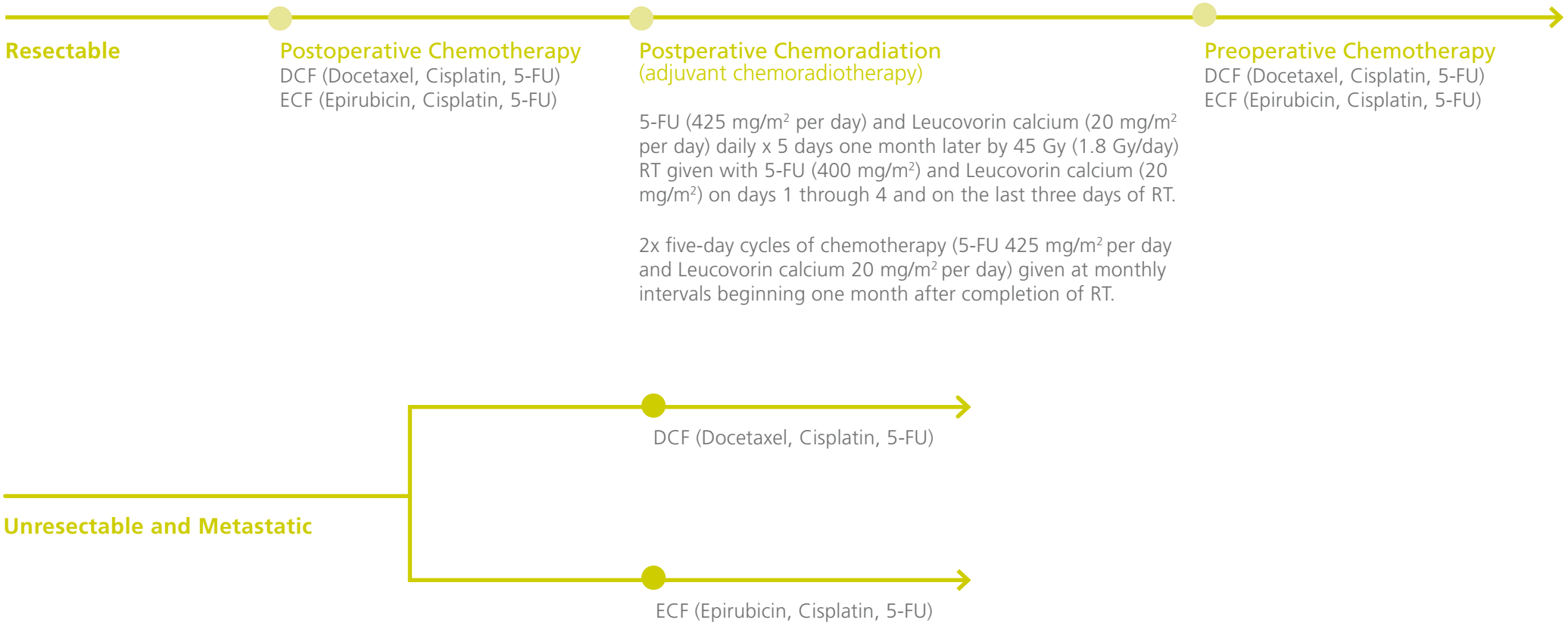
Hepatocellular Carcinoma

Would recommend following BCLC staging and treatment recommendations

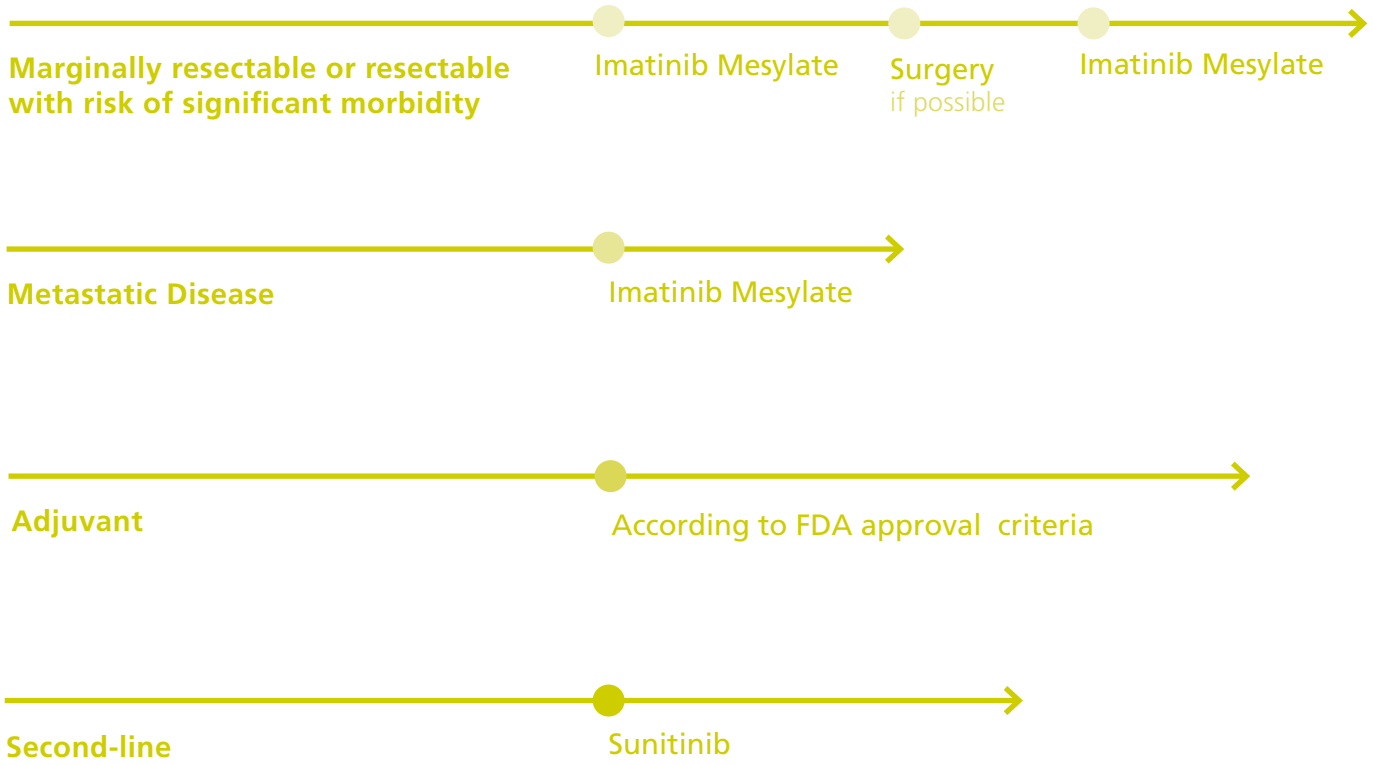
Localized unresectable → Chemoembolization (Doxorubicin)
Sorafenib for metastatic hepatocellular carcinoma excluding Child-Pugh Class C disease

Small Intestine Carcinoma

Gastric Carcinoma and GE Junction



Gastrointestinal Stromal Tumor



06 UG tumors and Soft Tissue Sarcomas

Urothelial tumors

Non-Seminomatous Germ Cell Tumors

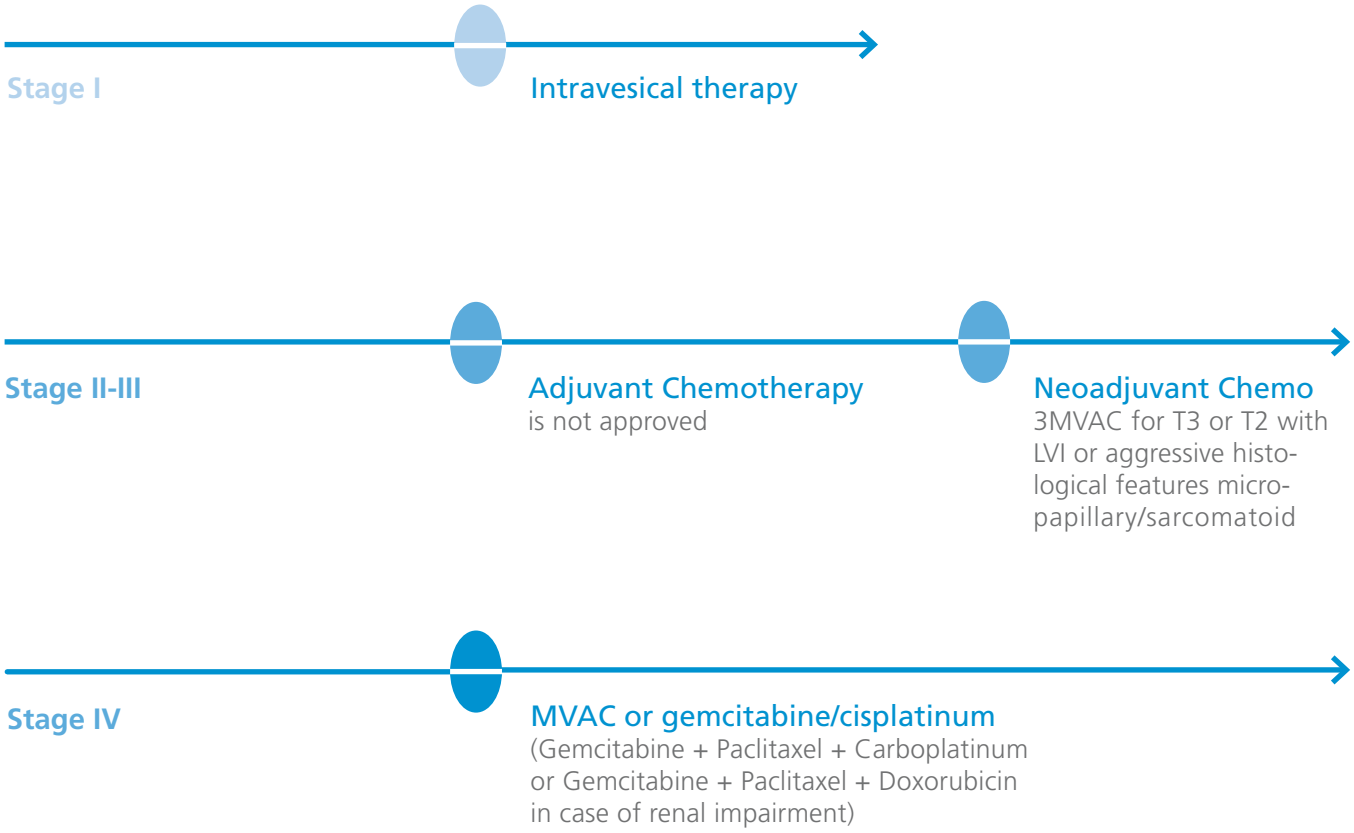
Seminoma

Renal Cell Carcinoma

Prostate Cancer

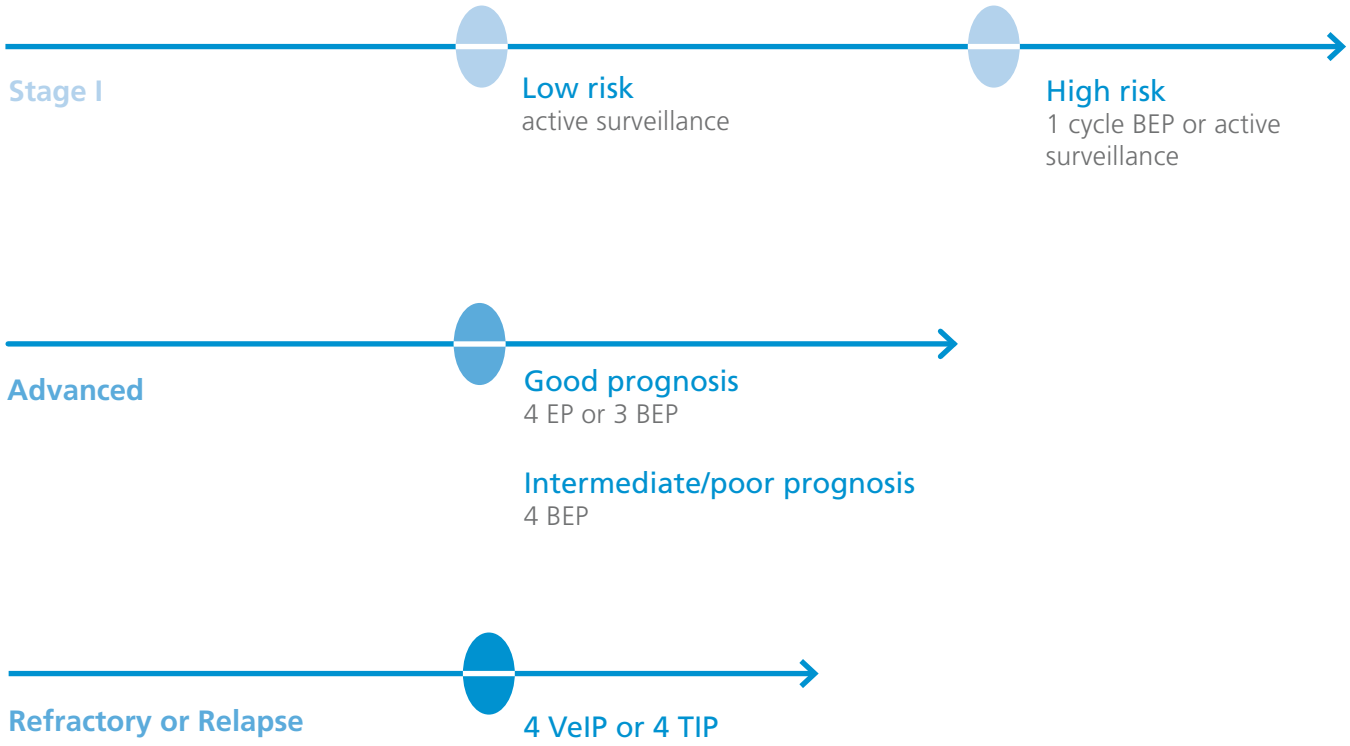
Soft tissue sarcoma
(limbs, retroperitoneum, pelvis)

Urothelial Tumors

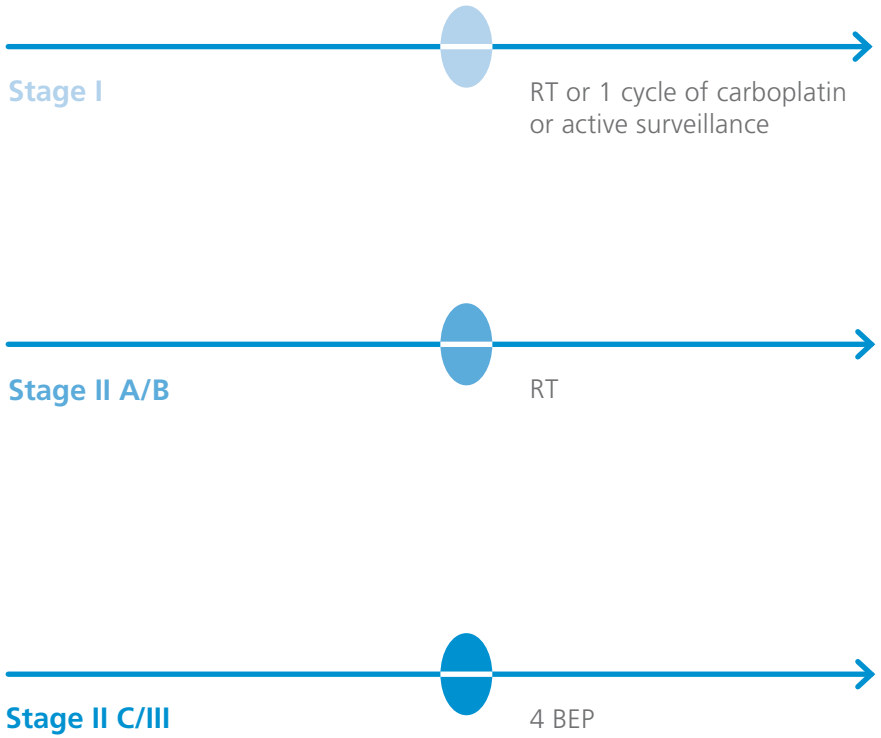


* No approved second-line

Non-Seminomatous Germ Cell Tumors



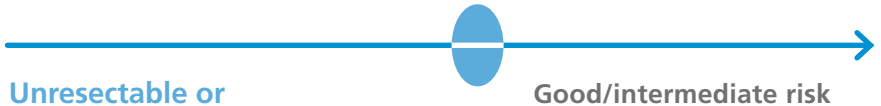
Seminoma


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

Poor risk
Temsirolimus 25 mg iv weekly

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

Soft Tissue Sarcoma (Limbs, Retroperitoneum, Pelvis)

Low grade

Surgery alone
Complementary radiotherapy is to be considered in special cases. No adjuvant CT

High grade resectable

Preoperative RT, CT or radiochemotherapy.
Complementary post surgical radiotherapy or chemotherapy could be considered

High grade unresectable

RT, CT or Chemoradiation

Relapsed, advanced, or metastatic

Chemotherapy including
Platinum, Ifosfamide, Doxorubicin. Liposomal Doxorubicin in kaposi sarcoma

07 Hematology Guidelines 2009

Diffuse large B cell non Hodgkin's lymphoma (CD20+)

Low grade non Hodgkin's lymphoma (CD20+)

Acute Myeloblastic Leukemia
Age < 65 years (except promyelocytic Leukemia)

Acute Myeloblastic Leukemia
Age > 65 years (except promyelocytic Leukemia)

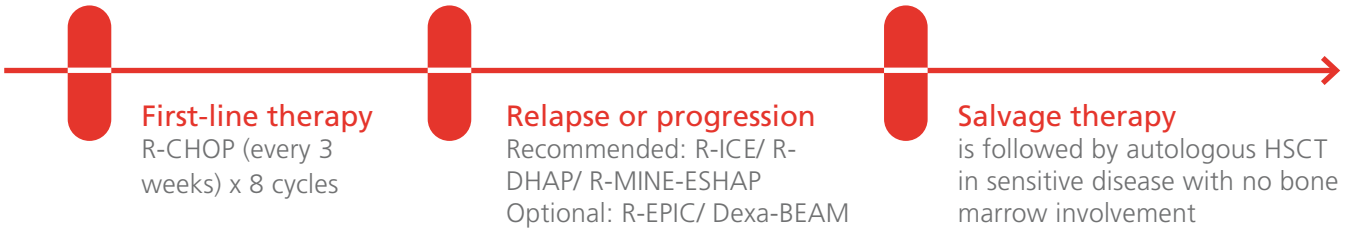
Hodgkin's lymphoma

B Chronic lymphocytic leukemia

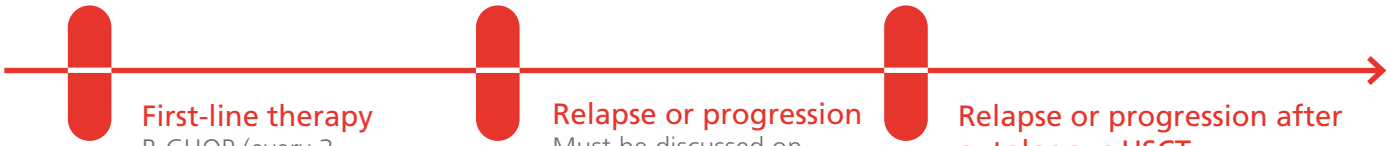
Chronic Myelogenous Leukemia (CML)

Myelodysplastic Syndromes

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



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



First-line therapy
R-CHOP (every 3 weeks) x 6 to 8 cycles

Relapse or progression
Must be discussed on individual basis

Relapse or progression after autologous HSCT
Consider for younger patients salvage therapy (including Anti CD20) followed by reduced intensity conditioning allogeneic HSCT from an HLA matched donor in sensitive or stable disease

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
Low	1
Intermediate	2
High	3

First-line therapy

indicated for high risk
Anti CD20 (375 mg/m^2)
+ chemotherapy
(Chloraminophene, CVP)

Radiotherapy if compressive lymph nodes

Maintenance after first-line therapy

Anti CD20 (375 mg/m^2) every 3 months during 2 years
only in follicular lymphoma responding to treatment

Relapse or progression

Interval treatment **relapse < 12 months**
Anti CD20 (375 mg/m^2) + Fludarabine based chemotherapy

Consider transplantation (reduced intensity conditioning allogeneic HSCT from an HLA matched donor or autologous HSCT if negative bone marrow)

Interval treatment **relapse ≥12 months**
Similar to first line therapy

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 (***good***)	Intermediate (***standard***)	Unfavorable (***high***)
Chromosomal Abnormality	→ t(8;21) (q22;q22) t(15,17) → inv16 (p13q22)/t(16;16) (p13;q22) → t(8,21) without del(9q) or complex karyotype	→ Normal Karyotype → t(9;11)(p22 ;q23) del(7q)- del(9q) -del(11q)- del(20q) -Y, +8, +11, +13, +21	→ 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		→ With no genetic alteration → Favorable: NPM1 mutation/FTL3- ITD- CEBPA mutation → Unfavorable: FLT3-ITD+MLL-PTD BAALC overexpression ERG overexpression	

Acute Myeloblastic Leukemia
age ≤ 60 years,except Promyelocytic Leukemia

First-line therapy induction therapy

Daunorubicin: 45-60 mg/ m^2/d, IV x 3 days

Cytarabine: 100 mg/ m^2/d, IV, CI x 7 days

Post remission therapy

Favorable risk ***(good),*** standard ***(intermediate)***
High dose Cytarabine (3 to 4 cycles)

Unfavorable ***(high)***
Allogeneic HSCT if HLA matched donor. Myeloablative or Reduced intensity conditioning

First relapse

< 6 months
Reinduction with high dose Cytarabine followed by allogeneic HSCT if sensitive relapse (myeloablative or reduced intensity conditioning)

Palliative care if comorbidities and/ or poor performance status

> 6 months
Reinduction plus Daunorubicine with high dose cytarabine followed by allogeneic HSCT if sensitive relapse (myeloablative or reduced intensity conditioning)

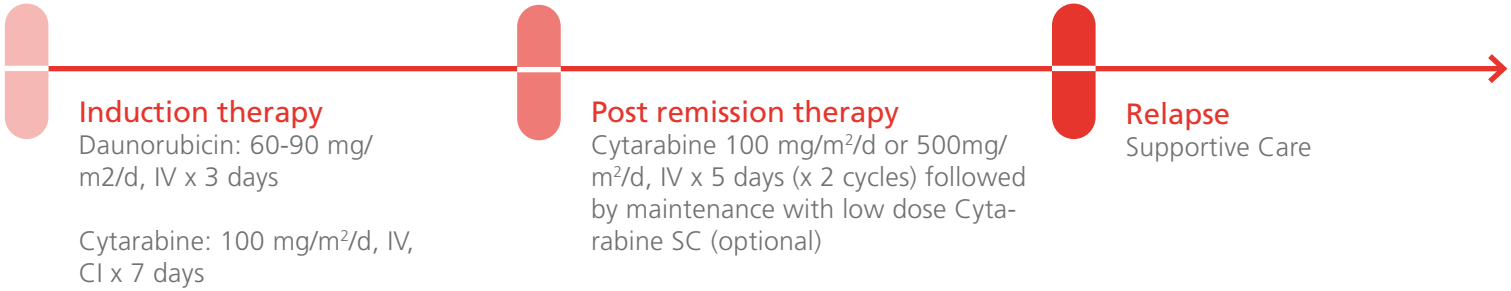
Subsequent relapses

If no prior transplant
Reinduction with high dose Cytarabine followed by allogeneic HSCT if sensitive relapse (myeloablative or reduced intensity conditioning)

Palliative care if comorbidities and/or poor performance status

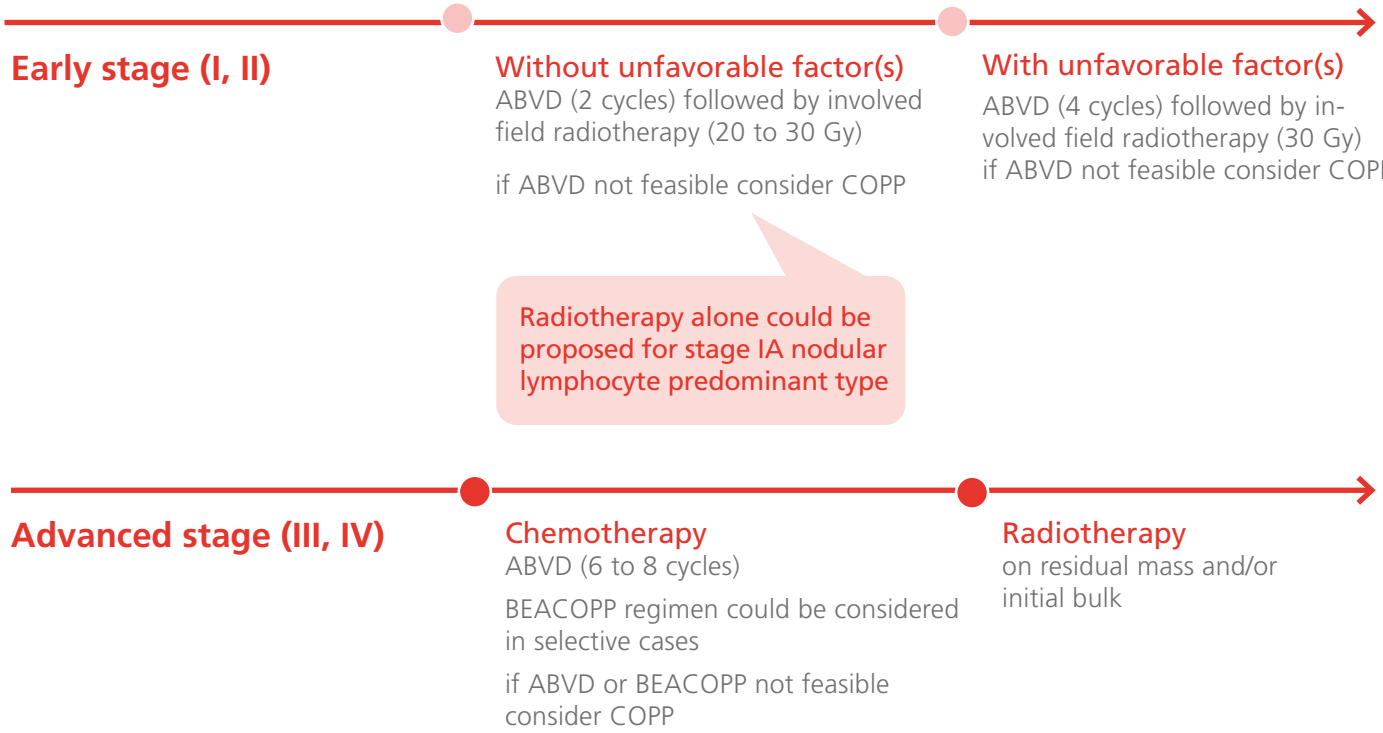
If prior transplant
Palliative Care

Acute Myeloblastic Leukemia
60 ≤ age ≤ 70 years, except Promyelocytic Leukemia



age > 70 years

Hodgkin's Lymphoma



Progression or Relapse

If primary therapy is radio-therapy alone
treatment as an advanced disease

If primary therapy is chemotherapy ± radiotherapy
Salvage non cross resistant chemotherapy: ICE / IVE/ ASHAP/ MIME/ Dexa-BEAM/ Ifos-famide +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

Bulky disease
mediastinal mass > 35% of the thoracic diameter

any other mass > 10 cm

ESR ≥ 50

B symptoms and ESR ≥ 30

> 3 sites

Extranodal sites

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, t(11q, v)

Prognosis

Unfavorable	Neutral	Favorable
T(11q;v)	Normal	del (13q)
del (11q)	+12	
del (17p)		
CD38 > 30%		CD38 < 30%
IgVH mutation ≤2%		IgVH mutation > 2%

Staging

Risk	Good	Intermediate	High
Rai System	0,I	II,III	IV
Binet System	A	B	C

First line therapy

Indication for treatment
Rai high risk/ Binet C/ unfavorable

For others consider treatment if
Autoimmune cytopenia
Recurrent infections requiring hospitalization more than 2 times during last 6 mo.
Bulky disease

Type of therapy
Chlorambucil
CVP
Fludarabine
Fludarabine + Cyclophosphamide (FC)

Relapse or Progression

Fludarabine + Cyclophosphamide + Anti CD20 (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)

Chronic Myelogenous Leukemia (CML)

First line treatment
Imatinib 400 mg daily for newly diagnosed in chronic phase

Intolerance or resistance to Imatinib
Dasatinib or Nilotinib
Interferon-α during pregnancy (if needed)

Alternative
consider Allo-SCT for low transplantation risk and high disease risk

Newly diagnosed accelerated phase
Imatinib 600mg/day, consider Dasatinib as an alternative and allogeneic stem cell transplantation for inadequate response.

Newly diagnosed blastic phase
treat as AML or ALL (depending on pathology) with added imatinib or dasatinib. Refer for allogeneic stem cell transplantation.

Myelodysplastic syndromes

Class of Drug/ Medication	Generic Name	Comments
Supportive Care		RBC transfusions as needed Platelet transfusions for overt bleeding or if platelets are <10
Hematopoietic growth factor	Erythropoietin (EPO)	Recommended for transfusion dependent anemia
Hematopoietic growth factor	Granulocyte-Colony Simulating Factor (G-CSF)	Used for neutropenic fevers
Immunomodulatory	Lenalidomide (Revlimid) 10 mg po/ day x 21 days CVV	Recommended only for low/int-1 transfusion-dependent 5q- MDS
Hypomethylating agent	5-azacitidine (Vidaza) 75 mg/ m^2/ day x 7 days SC (Q 4 weeks)	Recommended for int-1 and above MDS, or low risk MDS, highly transfusion dependent and not responding to other therapies
Immunosuppressive therapy	Horse or rabbit anti-thymocyte globulin (ATG), Cyclosporine	Recommended for young patients (<60) with low/int-1 MDS and hypocellular marrows
Iron chelator	Deferoxamine (Desferal) Deferasirox (Exjade)	Deferoxamine recommended for transfusion dependent patients with high ferritin levels. Deferasirox not recommended at the present time.
Chemotherapy	Cytarabine, Hydroxyurea etc.	Recommended for young patients with int-2 and above MDS not responding to hypomethylating drugs
Hematopoietic stem cell transplantation		Recommended for young patients with int-2 and above MDS or low risk MDS rapidly progressing to more advanced stages

Treatment options

IPSS	Tests	Recommendation
Low/Int1	Asymptomatic	Observation
Low/Int1, Anemia	EPO<300	Erythropoietin
	Hypocellular, age <60	ATG/cyclosporine
	5q- cytogenetics, no response to EPO (or EPO not indicated)	Lenalidomide
	EPO>300, not hypocellular or age >60, no 5q-	Supportive care
	Not responding to other therapy and requiring >4 units pRBC transfusions/month	Azacitidine
	Platelets<50	Azacitidine
	Transfusion dependent, Ferritin >1000	Iron chelation
Int-2/HR	Newly diagnosed	Azacitidine
	Age <60, resistant to hypomethylating drugs	Cytarabine based chemotherpy, SCT
	Age >60, resistant to hypomethylating drugs	Low dose cytarabine or supportive care
	Progressing from low risk/int-1, age <60	Cytarabine based chemotherpy, SCT
	Progressing from low risk/int-1, age >60	Azacitidine