ASU FC
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OESOPHAGEAL CANCER TREATMENT: overview of current status and recent updates.

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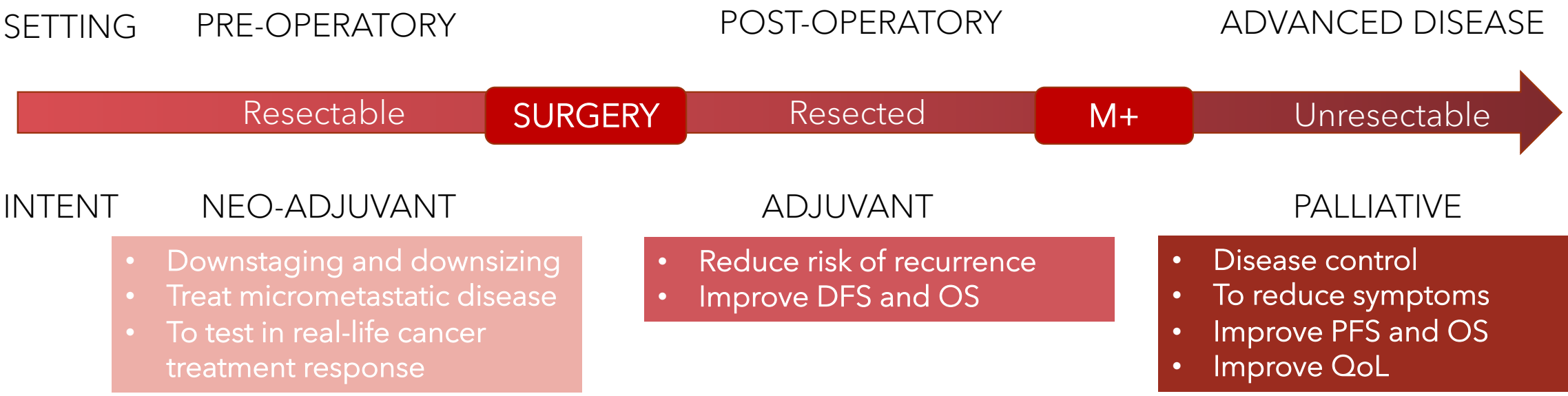
17th May 2025

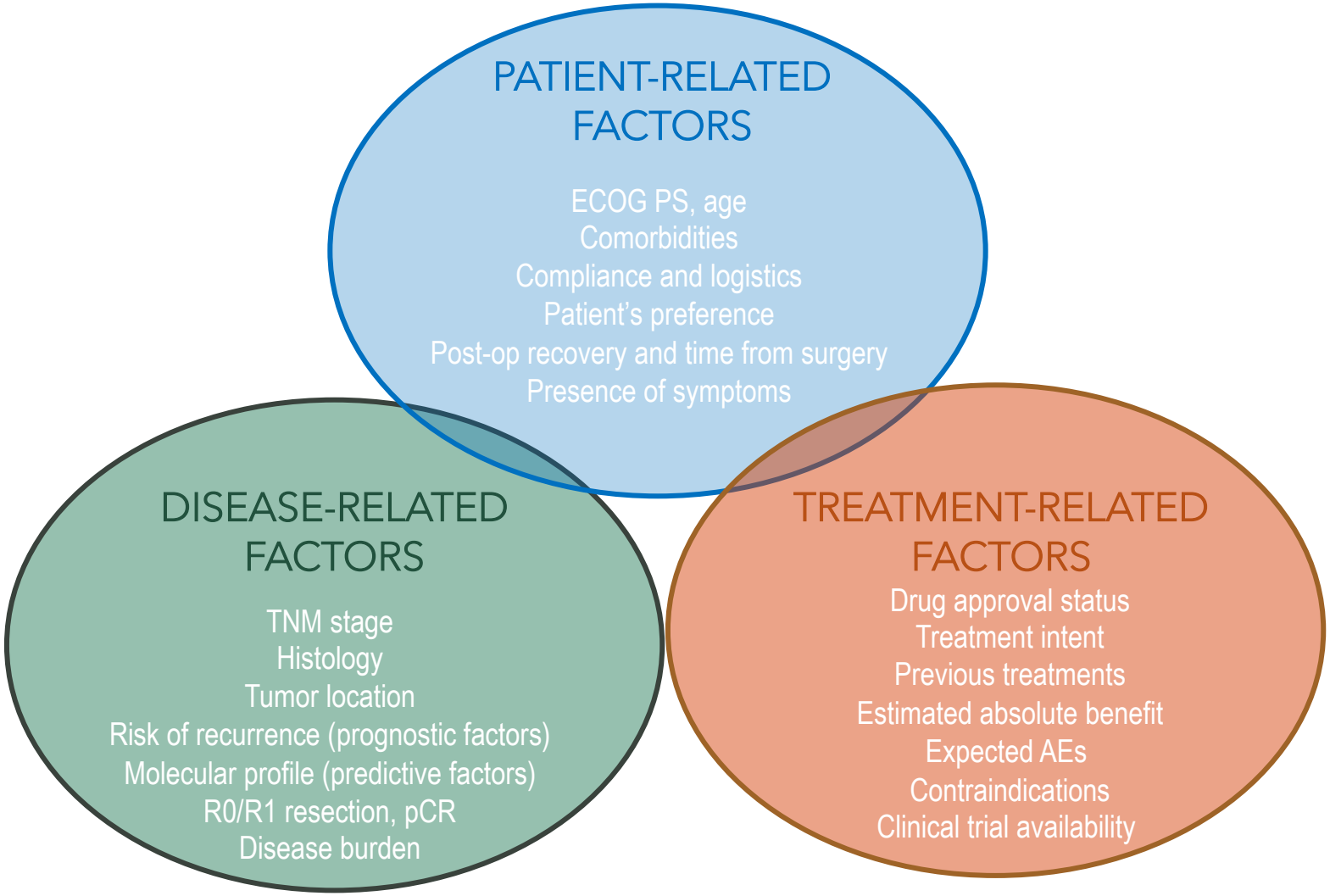
Topics

- Intent of cancer treatments according to disease setting
- Prognostic and predictive factors, clinical decision making algorithm
- Management of early and locally advanced oesophageal adenocarcinoma and SCC
- Management of advanced/unresectable oesophageal adenocarcinoma and SCC: first and further-line setting

Disease setting and treatment intent



How to choose the optimal treatment strategy?



GUIDELINES


Aiom
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ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE


NCCN
National Comprehensive
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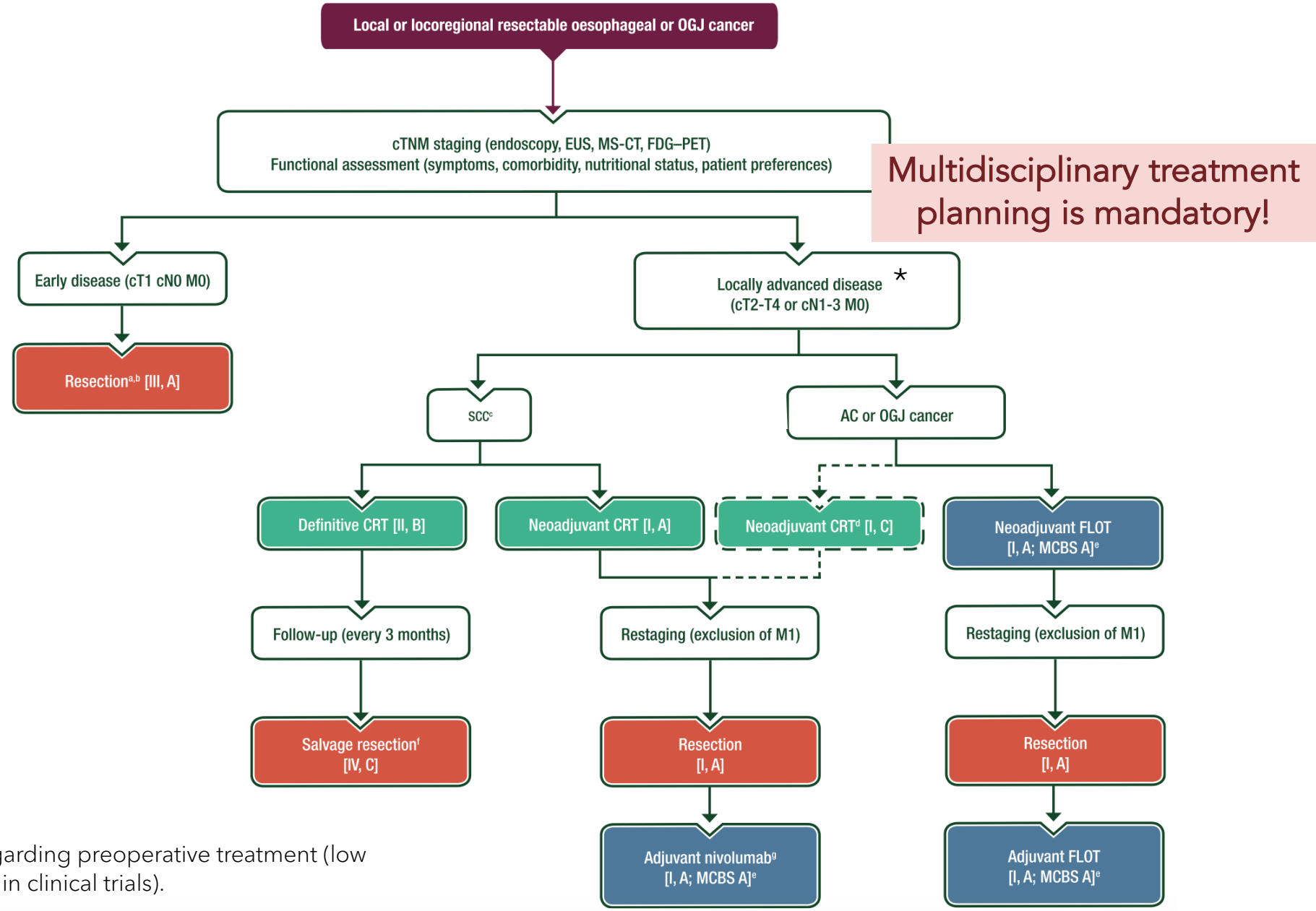
Management of early and locally advanced oesophageal cancer



Multidisciplinary treatment planning is mandatory!

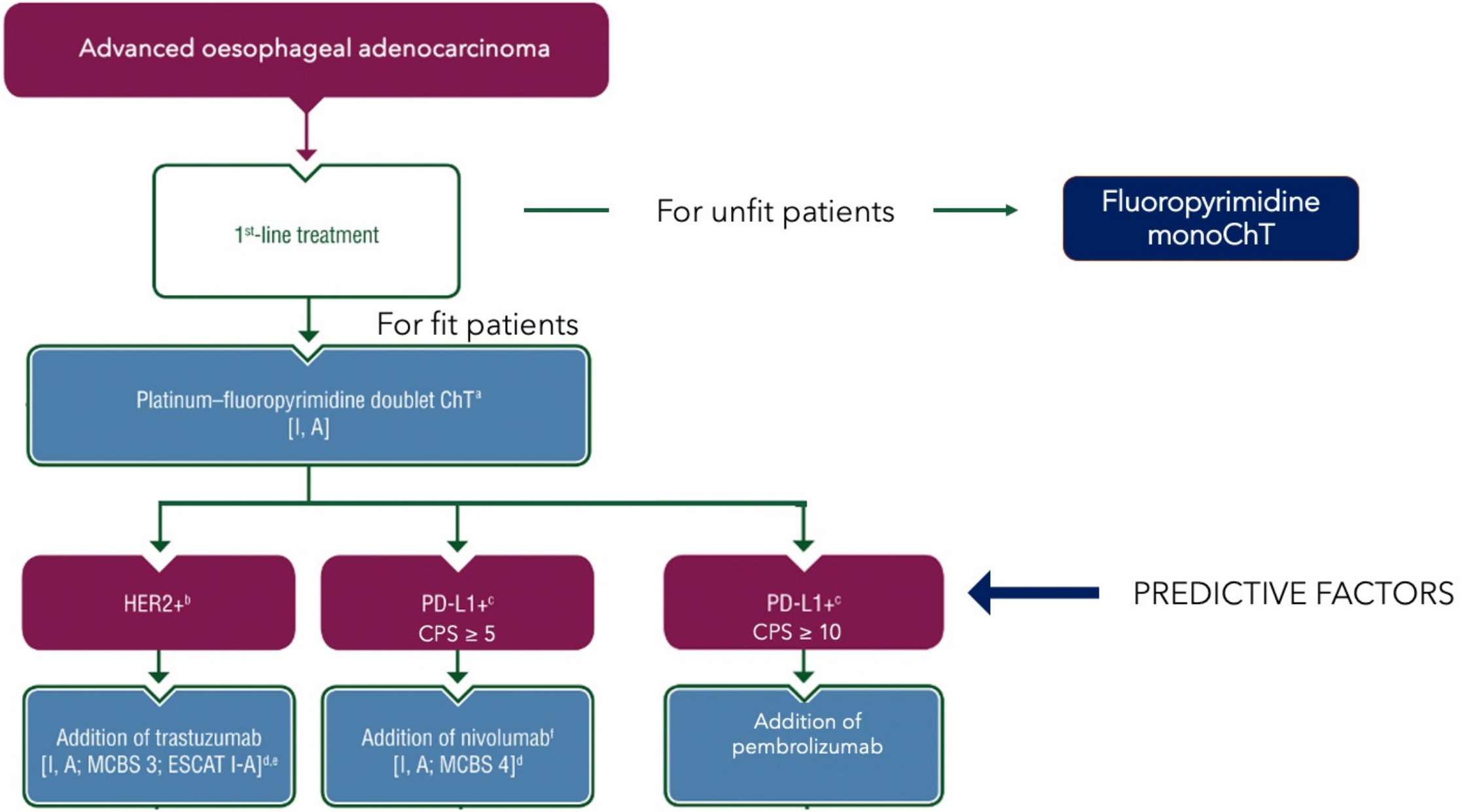
*cT2N0: controversy regarding preoperative treatment (low number of pts included in clinical trials).

From "ESMO Clinical Practice Guideline for oesophageal carcinoma – interim update 12th Feb 2025"

PREOP TREATMENT GOALS: rates of R0 surgical resections, DFS and OS.

Therapy	Disease setting	Trial	Control	Survival endpoints
FLOT	Locally advanced resectable gastric or GEJ AD	FLOT4 Phase II/III	ECF/ECX	mOS 50 vs 35 m
FLOT	Locally advanced resectable oesophageal AD	ESOPEC Phase III	CRT (CROSS)	mOS 66 vs 37 m 3y OS 57% vs 50% 5y OS 50% vs 38%
CRT (carboplatin + paclitaxel +RT	Locally advanced resectable oesophageal AD/SCC	CROSS Phase III	Surgery only	SCC: mOS 81.6 vs 21.1 m AD: mOS 43.2 vs 27.1 m
CRT (cisplatin + 5FU + RT)	Locally advanced resectable oesophageal AD/SCC	RTOG 85-01 Phase III	RT only	5y OS: 26% vs 0%
Nivolumab	Locally advanced oesophageal SCC/AD with no pCR after neoadj CRT	CheckMate 577 Phase III	Placebo	mDFS 22.4 vs 11 m

Management of advanced oesophageal adenocarcinoma: first-line therapy



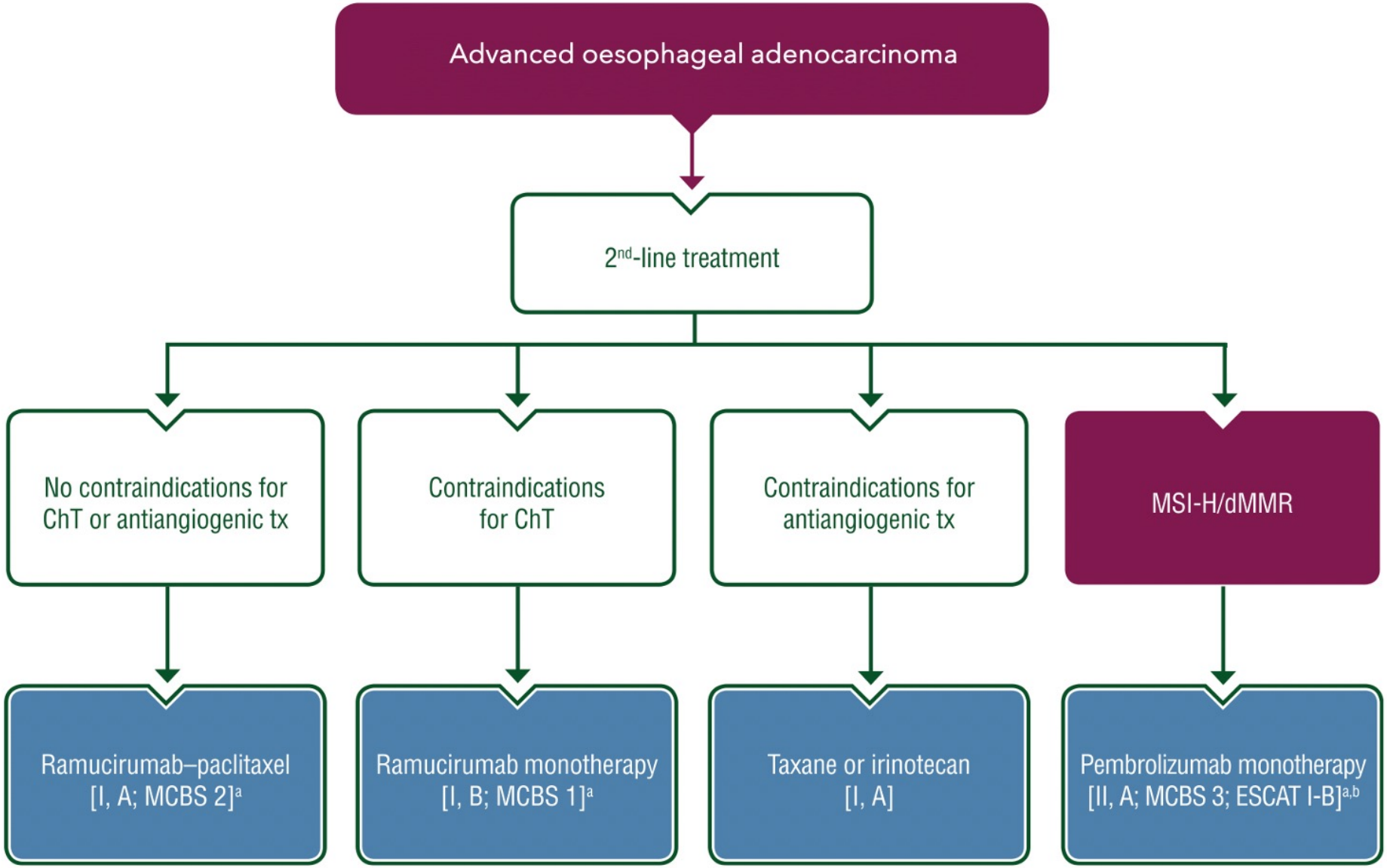
Adapted from ''Oesophageal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up''

Management of advanced oesophageal AD: first-line trials

TREATMENT GOALS: QoL, PFS and OS.

Therapy	Disease setting	Trial	Control	Survival endpoints
Nivolumab + fluoropyrimidine-platinum based ChT	HER2 neg advanced gastric, GEJ or oesophageal AD with PDL1 CPS ≥ 5	CheckMate 649 Phase III	ChT alone (FOLFOX/CAPOX)	mOS 13.1 vs 11.1 m
Pembrolizumab + cisplatin + 5FU	HER2 neg advanced Siewert I GEJ or oesophageal AD with PDL1 CPS ≥ 10	KEYNOTE-590 Phase III	Placebo + cisplatin + 5FU	mOS 12.4 vs 9.8 m
5FU + oxaliplatin	HER2 pos advanced gastric, GEJ or oesophageal AD	FLO vs FLP JCO 2008 Phase III	5FU + cisplatin	mOS 10.8 vs 8.8 m
Trastuzumab + fluoropyrimidine-platinum based ChT	HER2 pos advanced gastric or GEJ AD	ToGA Phase III	ChT	mOS 13.8 vs 11.1 m

Management of advanced oesophageal adenocarcinoma: second-line therapy



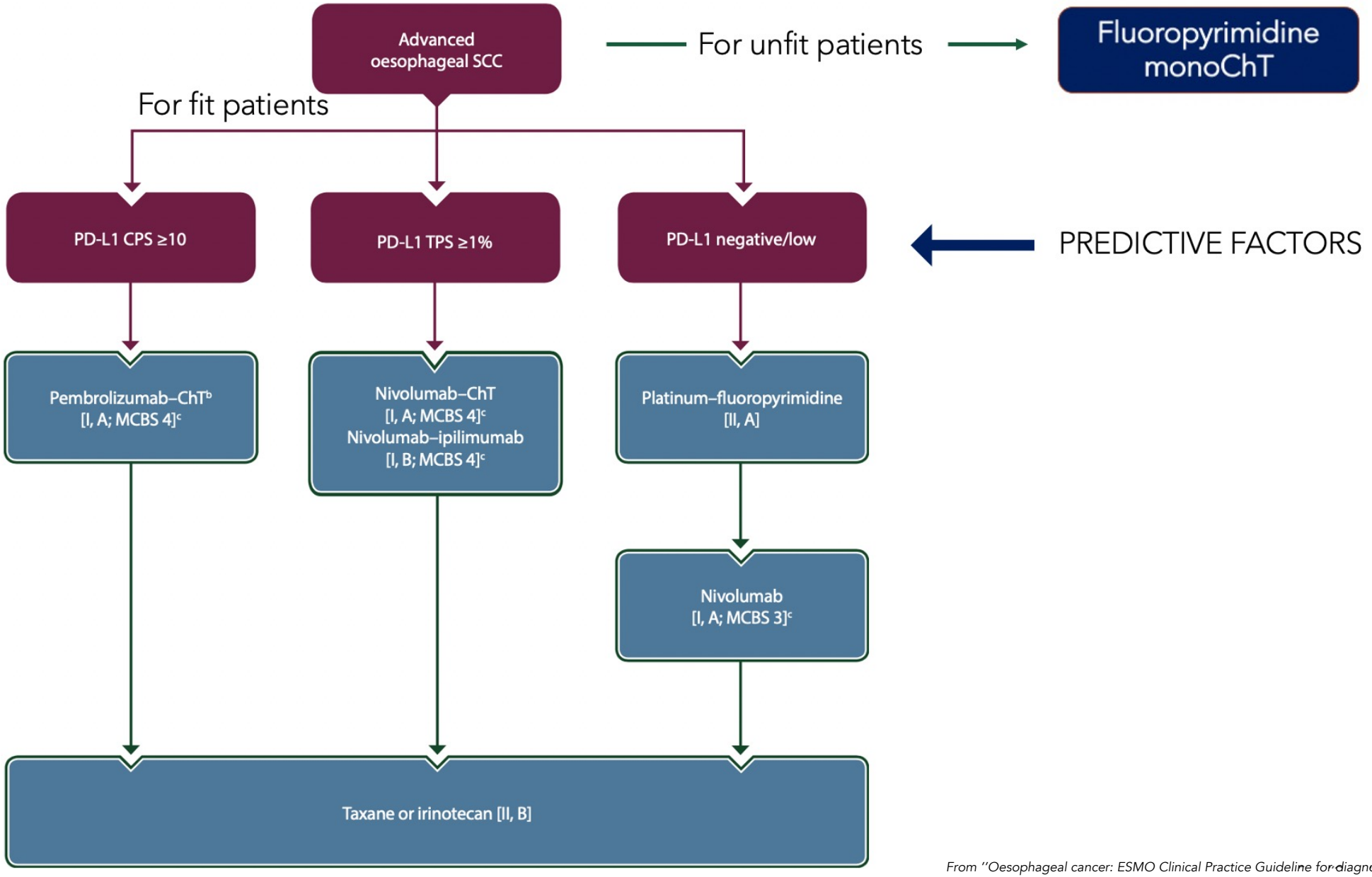
Adapted from ''Oesophageal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up''

Management of advanced oesophageal AD: second-line trials

TREATMENT GOALS: QoL, PFS and OS.

Therapy	Disease setting	Trial	Control	Survival endpoints
Ramucirumab + paclitaxel	Advanced gastric or GEJ AD after standard first-line	RAINBOW Phase III	Placebo + paclitaxel	mOS 9.6 vs 7.4 m
Ramucirumab	Advanced gastric or GEJ AD after standard first-line	REGARD Phase III	Placebo	mOS 5.2 vs 3.8 m
Docetaxel	Advanced oesophageal AD after standard first-line	COUGAR-02 Phase III	Placebo	mOS 5.2 vs 3.6 m
Fluoropyrimidine + irinotecan	Advanced gastric or GEJ AD after standard first-line	FFCD 0307 Phase III	ECX	mOS 9.5 vs 9.7 m
Pembrolizumab	Previously treated MSI-H solid tumors	KEYNOTE-158 Phase II (single arm)	//	mOS 23.5 m

Management of advanced oesophageal squamous carcinoma



From ''Oesophageal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up''

Management of advanced oesophageal SCC: first and second-line trials

TREATMENT GOALS: QoL, PFS and OS.

Therapy	Disease setting	Trial	Control	Survival endpoints
Nivolumab + fluoropyrimidine-platinum based ChT	Advanced oesophageal SCC with PDL1 TPS ≥ 1%	CheckMate 648 Phase III	ChT	mOS 15.4 vs 9.1 m
Ipilimumab + nivolumab	Advanced oesophageal SCC with PDL1 TPS ≥ 1%	CheckMate 648 Phase III	ChT	mOS 13.7 vs 9.1 m
Pembrolizumab + fluoropyrimidine-platinum based ChT	Advanced oesophageal SCC with PDL1 CPS ≥ 10	KEYNOTE-590 Phase III	Placebo + 5FU + cisplatin	mOS 13.9 vs 8.8 m
Nivolumab	Advanced oesophageal SCC after prior fluoropyrimidine-platinum ChT	ATTRACTION-3 Phase III	Taxane	mOS 10.9 vs 7.2 m

Conclusions and take-home messages: locally advanced setting

- **Multidisciplinary treatment** assessment and planning is mandatory.

- In locally advanced disease **preoperative treatment improves patients' overall survival**.

- Current standard of care in locally advanced setting:
  - SCC: definitive CRT with close surveillance and salvage surgery for local tumor persistence/progression or neoadjuvant CRT followed by surgery
  - AD: preoperative NACT (FLOT or FOLFOX for unfit pts) followed by surgery and post operative treatment; CRT must be reserved to pts unable/unwilling to undergo surgery

- Check nutritional status, long term treatment-related toxicities and symptoms of local and distant recurrence.

Conclusions and take-home messages: management of AD/SCC in advanced setting

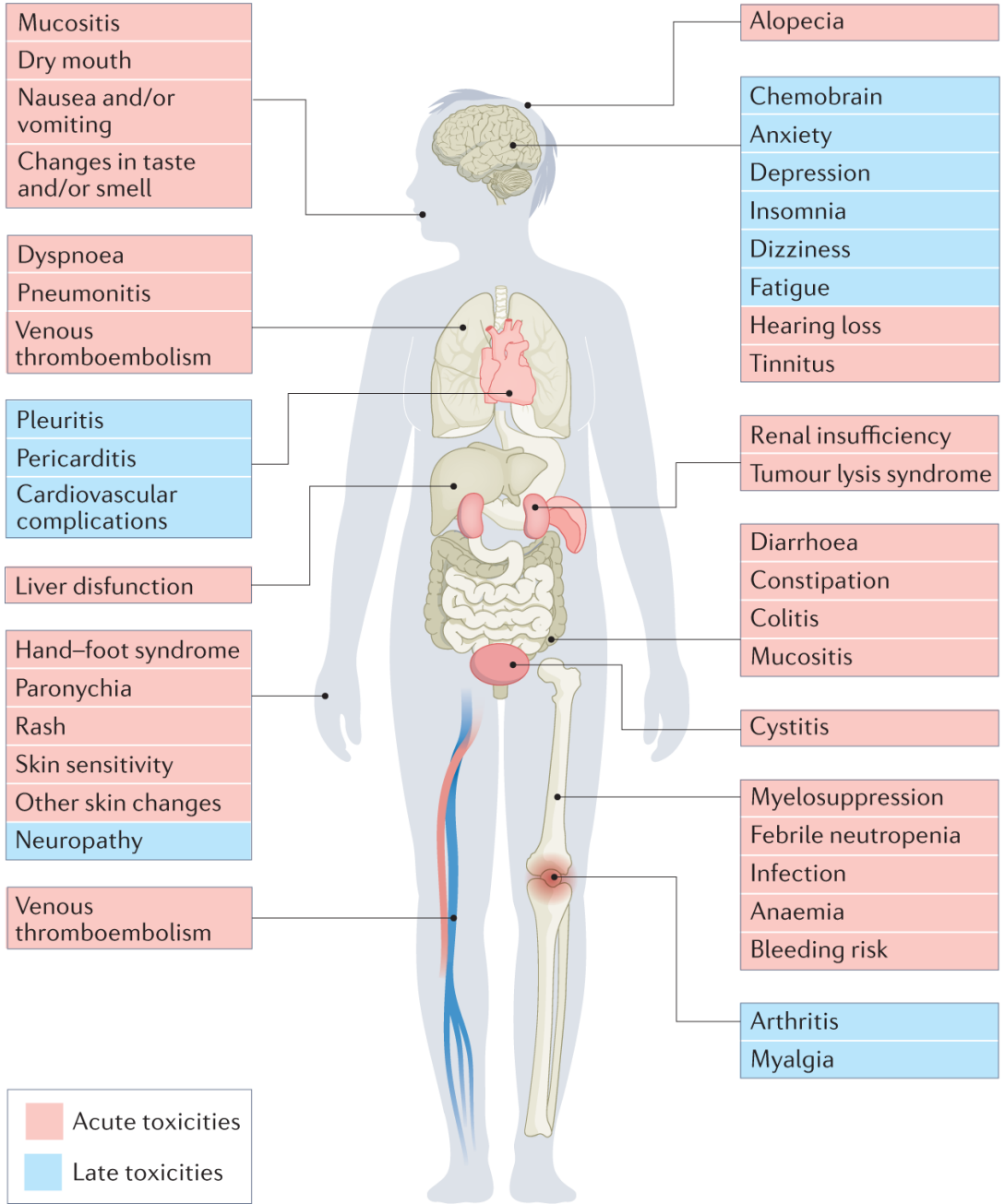
- Survival in clinical trials has historically been approximately 1 year.
- Early integration of **palliative care** improves clinical outcomes.
- Combination ChT over single-agent ChT improves survival.
- Standard first-line treatment options:

  Fit pts with AD: backbone ChT with **platinum-fluoropyrimidine doublet plus**
  - ✓ Anti HER2 Ab **Trastuzumab**: for HER2 pos disease
  - ✓ Anti PD-1 Ab **Nivolumab**: for PDL1 CPS ≥ 5 disease
  - ✓ Anti PD-1 Ab **Pembrolizumab**: for PDL1 CPS ≥ 10 disease

  Fit pts with SCC: backbone ChT with **platinum-fluoropyrimidine doublet plus**
  - ✓ Anti PD-1 Ab **Nivolumab**: for PDL1 TPS ≥ 1% disease
  - ✓ Anti PD-1 Ab **Pembrolizumab**: for PDL1 CPS ≥ 10 disease

  Elderly/unfit pts with AD/SCC: fluoropyrimidine monoChT.
- Second-line treatment must be reserved to fit patients as clinical benefit is modest.

Treatment-related toxicities: chemotherapy

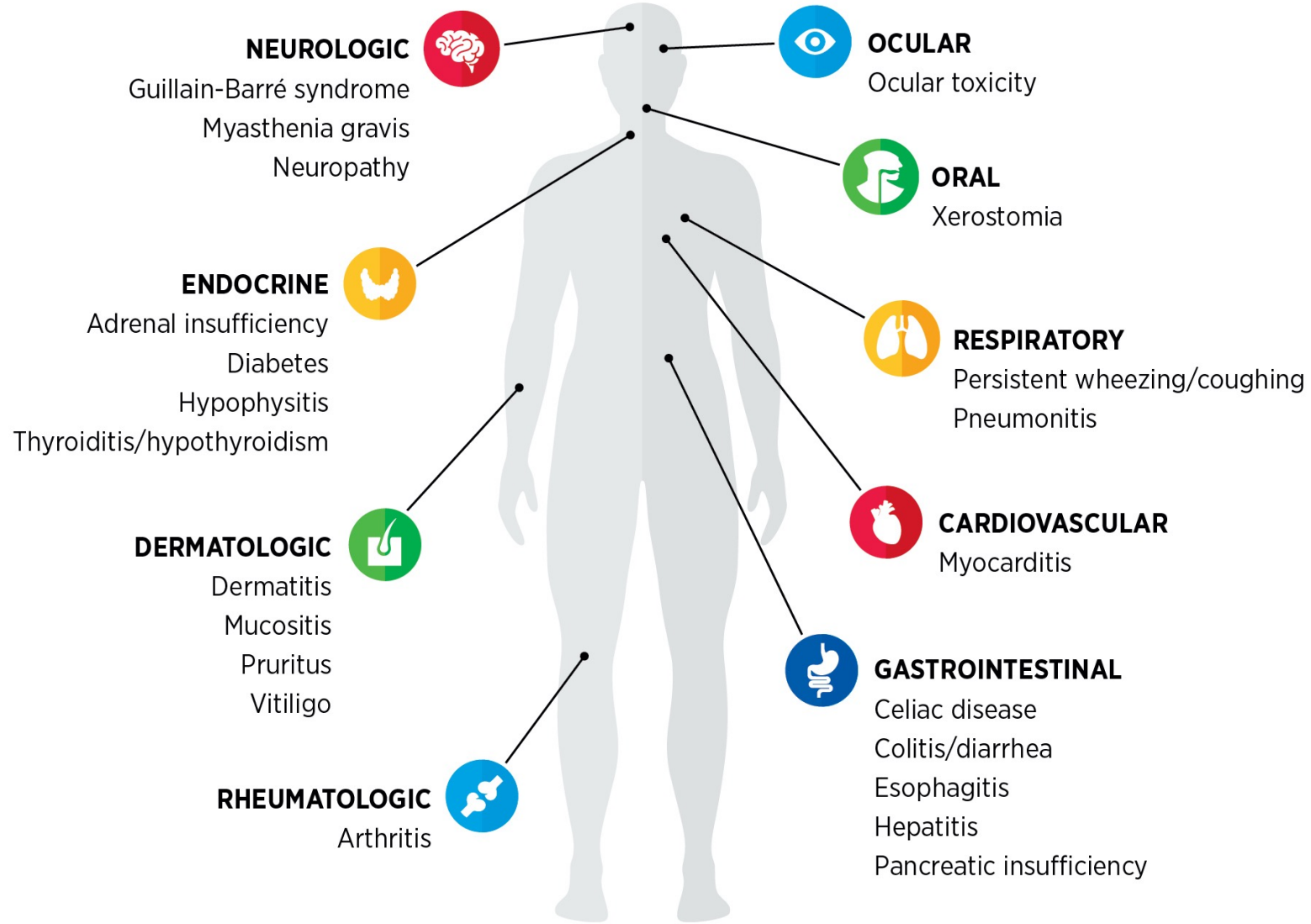


Focus on: Febrile neutropenia is defined as two consecutive readings of TC >38.0°C for 2 hours and an absolute neutrophil count (ANC) of <0.5 × 10^9/l, or expected to fall below 0.5 × 10^9/l.

It is one of the most serious and frequent complications from ChT.

From 'Mitigating acute chemotherapy-associated adverse events in patients with cancer. Nature Clin Rev Onc 2022'

Treatment-related toxicities: immunotherapy



irAEs potentially can affect any organ, with a broad spectrum of clinical manifestations (10% or severe AEs).

Possible overlap with AEs from ChT.

Patients are trained to recognize irAEs.

Early referral to the oncologist in case of clinical suspicion of irAEs: early detection improves clinical outcome!

From ''AACR Cancer Progress Report''

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GRAZIE PER L'ATTENZIONE

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