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Mayo Consensus on AL Amyloidosis: Diagnosis and Treatment

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AL Amyloidosis Diagnosis

- **The diagnosis of systemic amyloidosis requires the presence of all of the following:**
  - **Presence of amyloid-related systemic syndrome (such as renal, liver, heart, gastrointestinal tract or peripheral nerve involvement)**
  - **Positive amyloid staining by Congo Red or EM in any tissue**
  - **Clear evidence that amyloid is immunoglobulin related by direct sub-typing of amyloid deposits (Mass spectroscopy is standard approach at our institution)**
  - **Evidence of a monoclonal plasma cell proliferative disorder (any or all of the following: serum or urine M protein, abnormal free light chain ratio or clonal plasma cells in bone marrow)**
- **Localized forms of amyloidosis (such as tracheobronchial, genitourinary, isolated carpal tunnel and non-purpuric cutaneous lesions) do not require systemic therapy**
- **The recommendations presented herein are a general approach. However, clinical trials are preferred at every step.**

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ASCT Transplant Eligibility Criteria

- "Physiologic" Age ≤ 70 years
- Performance Score ≤ 2
- Systolic BP ≥ 90 mmHg [a]
- TnT < 0.06 ng/ml (or hs-TnT < 75 ng/ml)
- CrCl ≥ 30 ml/min [b] (unless on chronic dialysis)
- NYHA Class I/II

[a] Caution as well for patients with BP <100 mmHg
[b] Selected patients may become eligible for ASCT with cardiac and renal transplantation

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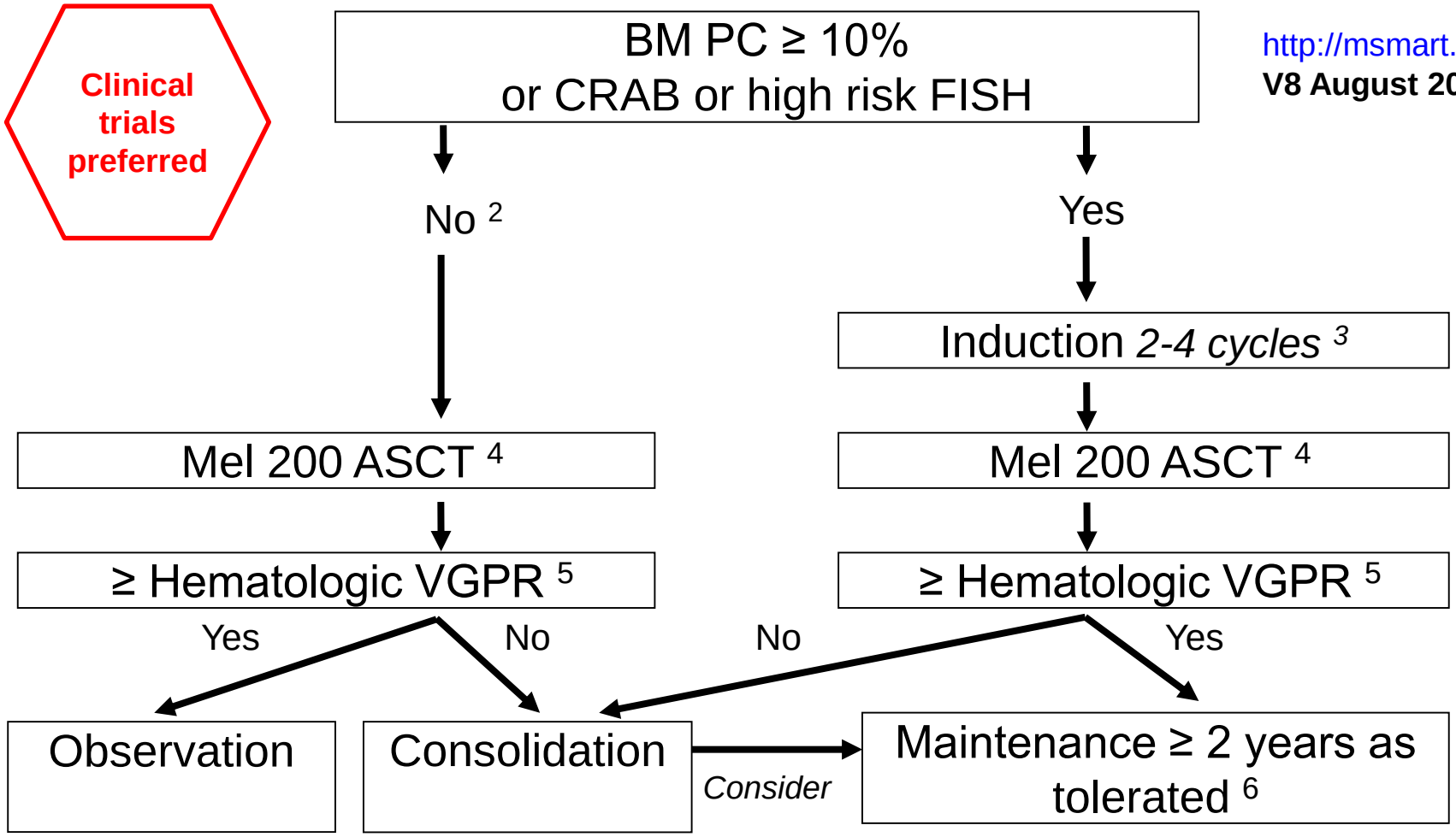
Newly Diagnosed AL Amyloidosis[1] - Transplant eligible



1 Consider adding doxycycline for at least a year
2 Induction (CyBorD or low-dose lenalidomide VRd) also used if delay (e.g. >1 month) in proceeding to ASCT
3 If CR, collect stem cells and option to observe without ASCT
4 For CrCl <30, use Mel 140 mg/m2. Age >70, consider Mel 140
5 Decision to change/add therapy if > CR made based on a number clinical factors. Re-refer to amyloid center of excellence
6 If high-risk FISH (del 17p, t(4;14), or t(14;20)), use proteasome inhibitor for maintenance; otherwise lenalidomide

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Newly Diagnosed AL Amyloidosis[1] - Transplant ineligible

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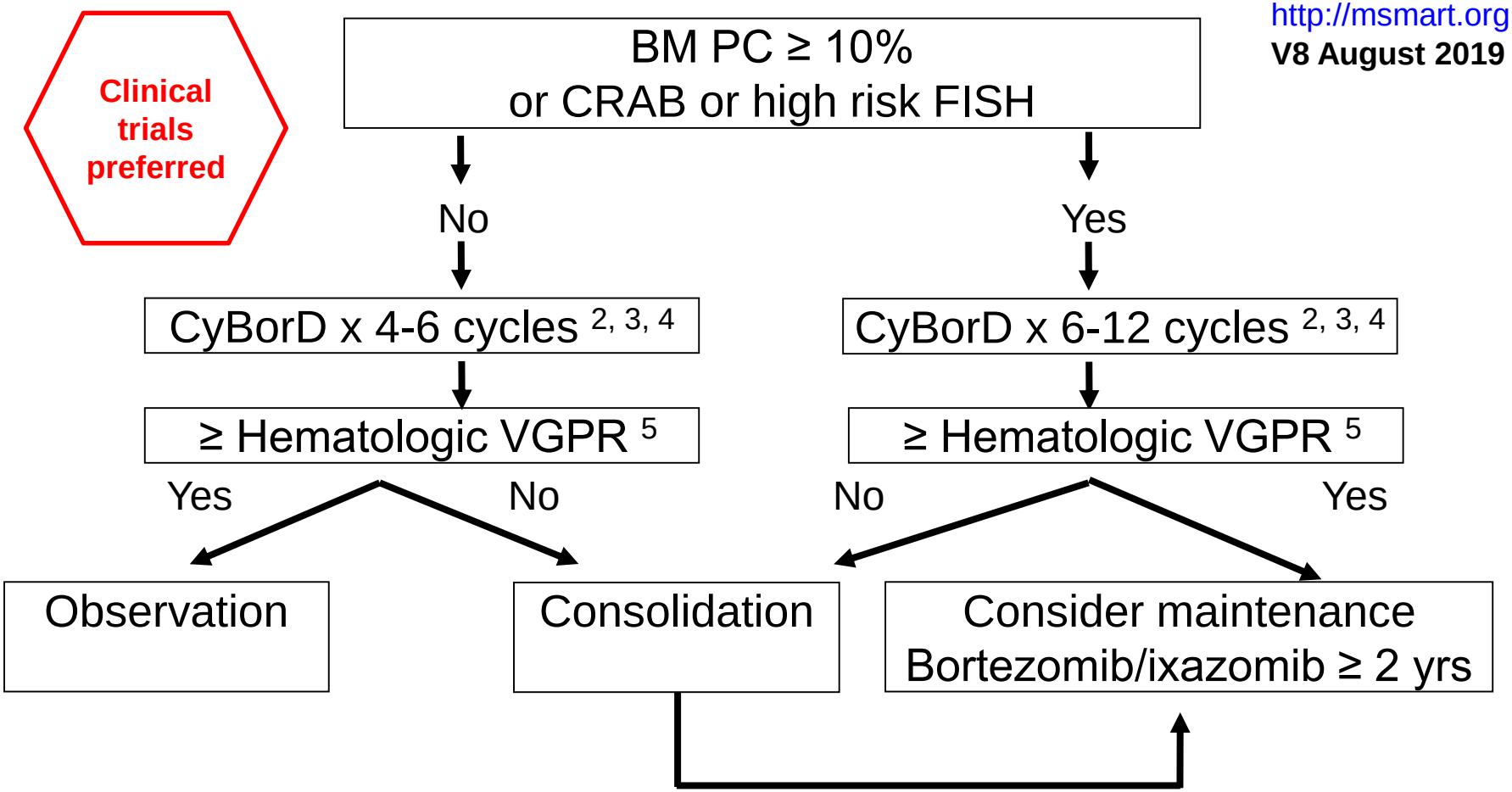

1 Consider adding doxycycline for at least a year
2 Or BMel-Dex
3 If < PR at 2 months consider changing therapy
4 If young, consider stem cell collection for eventual ASCT
5 Decision to change/add therapy if > CR made based on a number clinical factors. Re-refer to amyloid center of excellence

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Treatment of AL – off study

Clinical trials preferred

Relapsed/ Refractory AL Amyloidosis

2nd line

Dara or dara-based therapies

Heme relapse ≥ 2 years after last therapy

Consider repeating original therapy

Not bortezomib refractory

CyBorD or B-Mdex[1] or Vd

Bortezomib refractory

3rd line

Pom-Dex or Len[2] -Dex

4th line

Paucity of data, but carfilzomib[3] or venetoclax[4]-based therapies can be considered

[1] Melphalan and dex doublet very appropriate if patient has significant peripheral neuropathy
[2] Starting dose of lenalidomide should be no higher than 15 mg
[3] Not recommended in patients with cardiac involvement
[4] Be very cautious of infection risk
Dara, daratumumab; Vd, bortezomib+dex; Len, lenalidomide; Pom, pomalidomide

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