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mSMART

Mayo Consensus on AL Amyloidosis: Diagnosis, Treatment and Prognosis

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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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Hematological and organ response assessment

Response type	Criteria
HEMATOLOGIC RESPONSE[1]	
Complete response (CR)	Negative serum and urine IFE and Normal serum immunoglobulin κ/λ FLC ratio
Very good partial response (VGPR)	dFLC < 40 mg/L
Partial response (PR)	dFLC decrease of greater than 50%
No response (NR)	Less than a partial response
ORGAN RESPONSE[1,2,3]	
Cardiac response	Decrease of NT-proBNP by >30% and 300 ng/L (if baseline NT-proBNP >650 ng/L)
Renal response	At least 30% decrease in proteinuria or drop below 0.5 g/24 hour, in the absence of renal progression defined as a >25% decrease in eGFR
Hepatic response	50% decrease in abnormal alkaline phosphatase value or decrease in radiographic liver size by at least 2 cm

dFLC, difference between involved and uninvolved serum immunoglobulin free light chain;
a value adequate to measure response is deemed to be 50 mg/L

[1]Palladini et al, *J Clin Oncol,* 2012;30:4541-9
[2]Gertz et al, *Am J Hematol,* 2005;79:319-28
[3]Palladini et al, *Blood*, 2014;124:2325-32

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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 SBP <100 mmHg
[b] Selected patients may become eligible for ASCT with cardiac and renal transplantation

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Newly Diagnosed AL Amyloidosis - Transplant eligible

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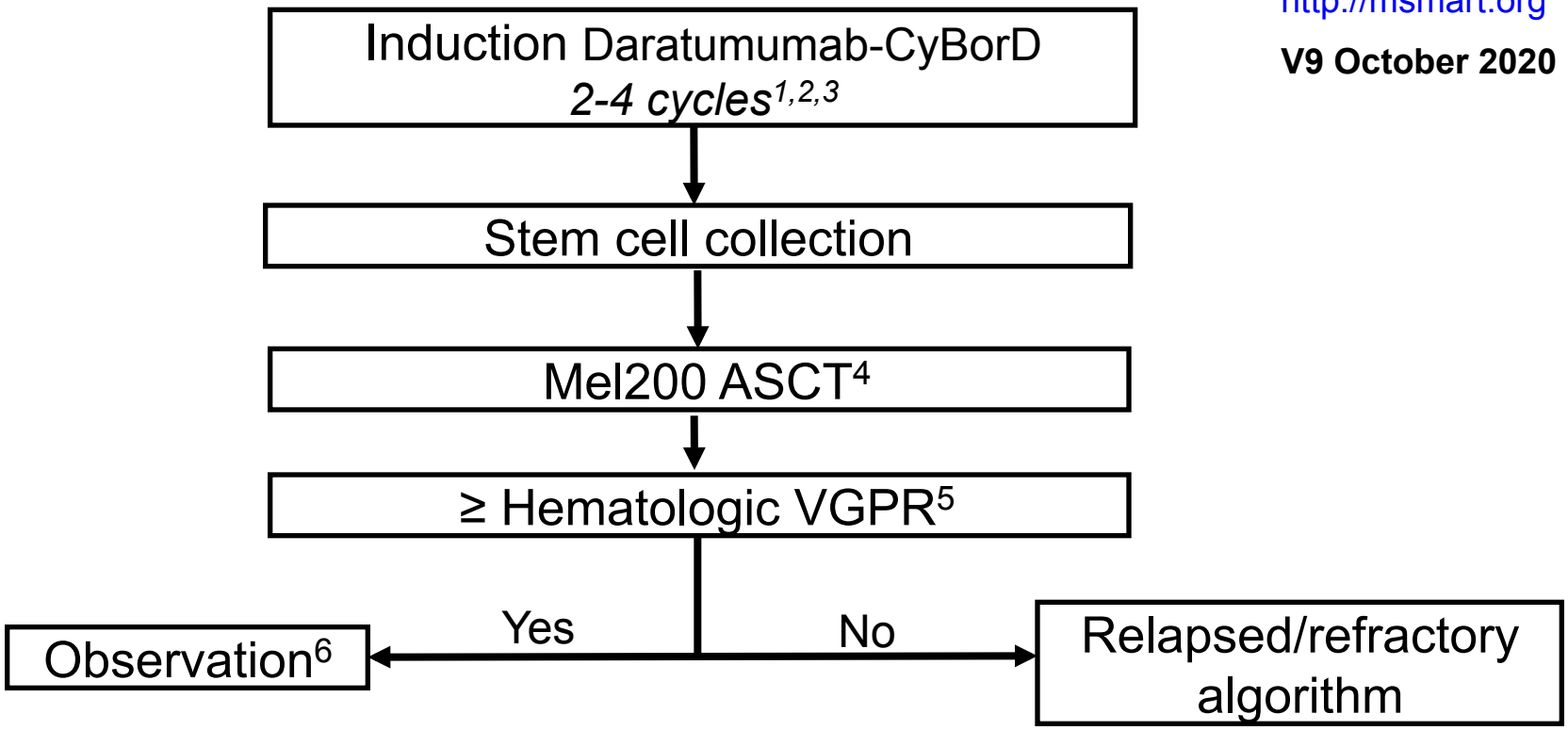

[1]Consider adding doxycycline for at least a year
[2]If daratumumab is not accessible, CyBorD is an acceptable alternative regimen (weekly bortezomib only)
[3]If CR, option to observe without ASCT for patients with low disease burden and proceed as transplant ineligible algorithm
[4]For CrCl <30, use Mel 140 mg/m2
[5]Decision to change therapy if in VGPR but < CR is based on a number clinical factors. Re-refer to amyloid center of excellence
[6]For patients with overt multiple, use myeloma-type maintenance; consider for BMPCs ≥20% and high-risk FISH (del 17p, t(4;14), t(14;16) and t(14;20)). Please refer for myeloma mSMART guidelines for choice of maintenance

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Newly Diagnosed AL Amyloidosis - Transplant ineligible#

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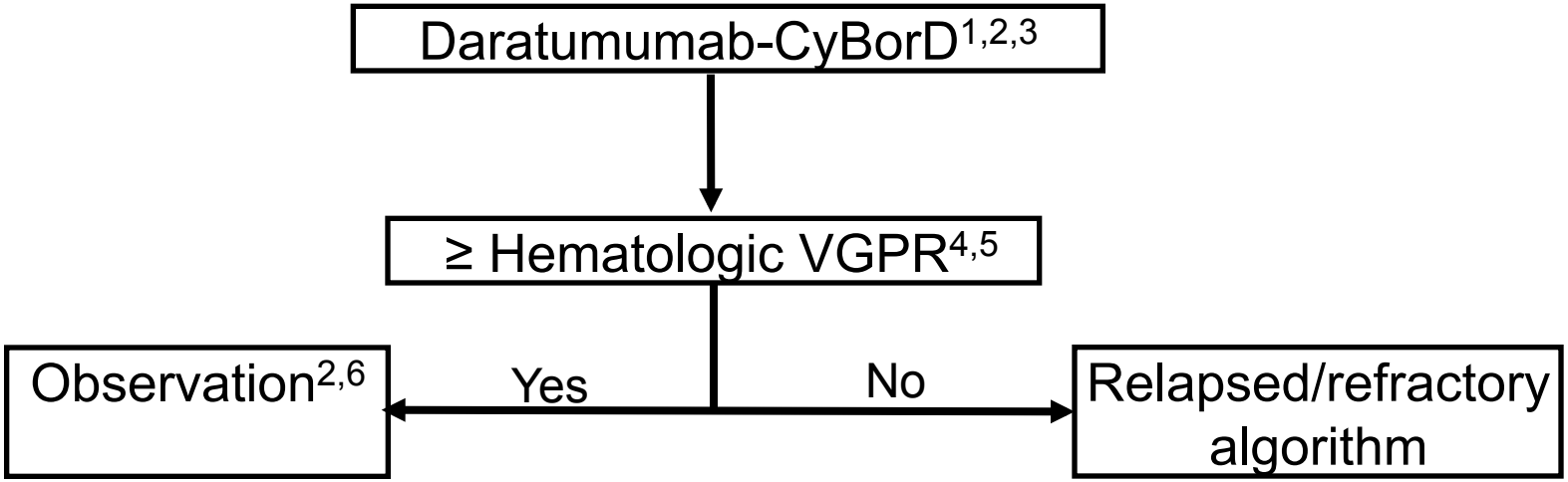

[1]Consider adding doxycycline for at least a year

[2]If daratumumab-CyBorD, 6 cycles followed by daratumumab monotherapy, completing up to 24 cycles. If daratumumab is not accessible, CyBorD or BMDex for 6-12 cycles are acceptable alternative regimens (weekly bortezomib)

[3]If young, consider stem cell collection for eventual ASCT if eligibility for transplant is foreseeable

[4]If < PR at 2 months or < VGPR within 4 cycles change therapy, unless signs of organ response are seen

[5]Decision to change therapy if in VGPR but < CR is based on a number clinical factors. Re-refer to amyloid center of excellence

[6]Only for patients with overt multiple myeloma, BMPCs ≥20% or high-risk FISH and who are not receiving extended duration daratumumab, consider maintenance. Lenalidomide should not be used in patients with advanced heart or autonomic nerve involvement

#For IgM AL amyloidosis consider referral to amyloidosis center due to a more challenging management

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Treatment of relapsed/refractory AL amyloidosis

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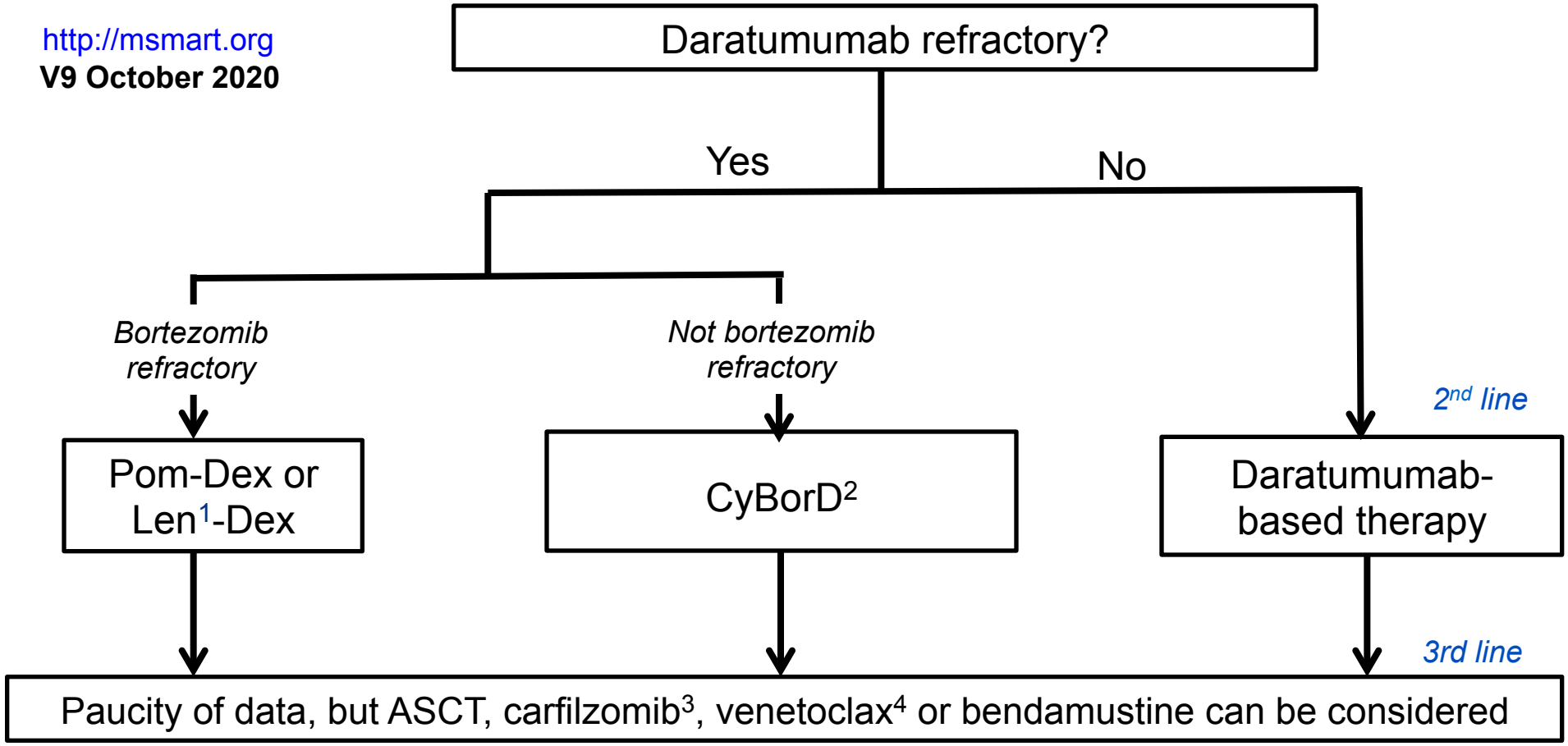

[1]Starting dose of lenalidomide should be no higher than 15 mg/d
[2]Melphalan-dexamethaone or Ixazomib-dexamethasone are appropriate if patient has significant neuropathy
[3]Not recommended in patients with cardiac involvement
[4]For patients with t(11;14). Be cautious of infection risk.

ASCT, autologous stem cell transplant; Len, lenalidomide; Pom, pomalidomide; Dex, dexamethasone