POEMS Syndrome

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POEMS Syndrome

Also known as…
Osteosclerotic Myeloma
Crow-Fukase syndrome
and Takatsuki syndrome

- **P**olyneuropathy
- **O**rganomegaly
- **E**ndocrinopathy
- **M**onoclonal protein
- **S**kin changes

Clinical Features*

- N = 99 patients
- Median age: 51 years
- Male gender in 63% pts
- Neuropathy is the dominant characteristic
- Only 29 patients had a “complete” POEMS syndrome
- 18 patients developed new manifestations over time
- Infrequent progression to overt MM

*Dispenzieri et al, Blood 2003

POEMS Diagnostic Criteria*

Mandatory major criteria	1. **P**olyneuropathy 2. **M**onoclonal PC proliferative disorder
Major criteria	3. Sclerotic bone lesions 4. Castleman disease 5. Increased levels of VEGF-α
Minor criteria	6. **O**rganomegaly or lymphadenopathy 7. Extravascular volume overload 8. **E**ndocrinopathy 9. **S**kin changes 10. Papilledema 11. Thrombocytosis/polycythemia

Required:
- both mandatory major criteria
- 1 major criteria
- and at least 1 minor criteria

Diabetes and thyroid abnormalities by itself are not enough as endocrinopathy

* Dispenzieri A, Am J Hematol 2011;86:591-601

Other Symptoms and Signs

- Clubbing
- Weight loss
- Hyperhidrosis
- Pulmonary hypertension / restrictive lung disease
- Thrombotic diathesis
- Diarrhea

Mandatory Major Diagnostic Criteria

- Sensorymotor peripheral neuropathy
  (typically demyelinating with axonal loss)

- Monoclonal plasmaproliferative disorder
  (almost always lambda, usually IgA-lambda, and BMPC <10%)

⇨ Biopsy of an sclerotic lesion is not imperative in the proper clinical context

Utility of VEGF in POEMS*
(both serum or plasma levels)

- **Differential diagnosis** with other plasma cell dyscrasias, neuropathic processes and multisystem diseases
  - Chronic inflammatory desmyelinating polyradiculoneuropathy

    (CIDP ≠ POEMS also by nerve conduction study/EMG**)
  - MGUS neuropathy
  - AL neuropathy
  - Castleman's disease variant of POEMS syndrome

    (no PC dyscrasia, little/no PN, but several of the minor criteria)

- **Monitoring disease activity** after treatment (correlates with clinical improvements better than hematologic response)

* D'Souza A et al (Mayo Clinic), Blood 2011.
** Mauermann ML et al (Mayo Clinic), J Neurol Neurosurg Psychiatry 2012.

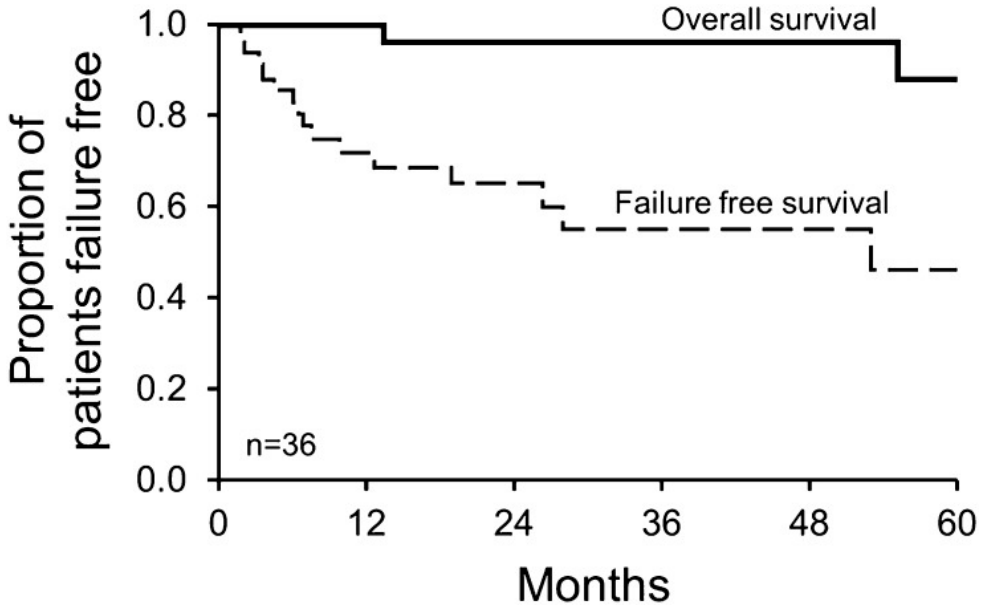
Assessment of Response / Progression (after ASCT)*

	Response	Progression / relapse
Clinical	Any objective improvement	Any objective worsening
Hematologic	= MM	= MM
VEGF (if baseline ≥ 200 pg/mL)	↓ at least 50%	↑ to ≥ 200 pg/mL
PET	↓ at least 50%	Definite ↑ in size or FDG avidity or new lesions (FDG+)

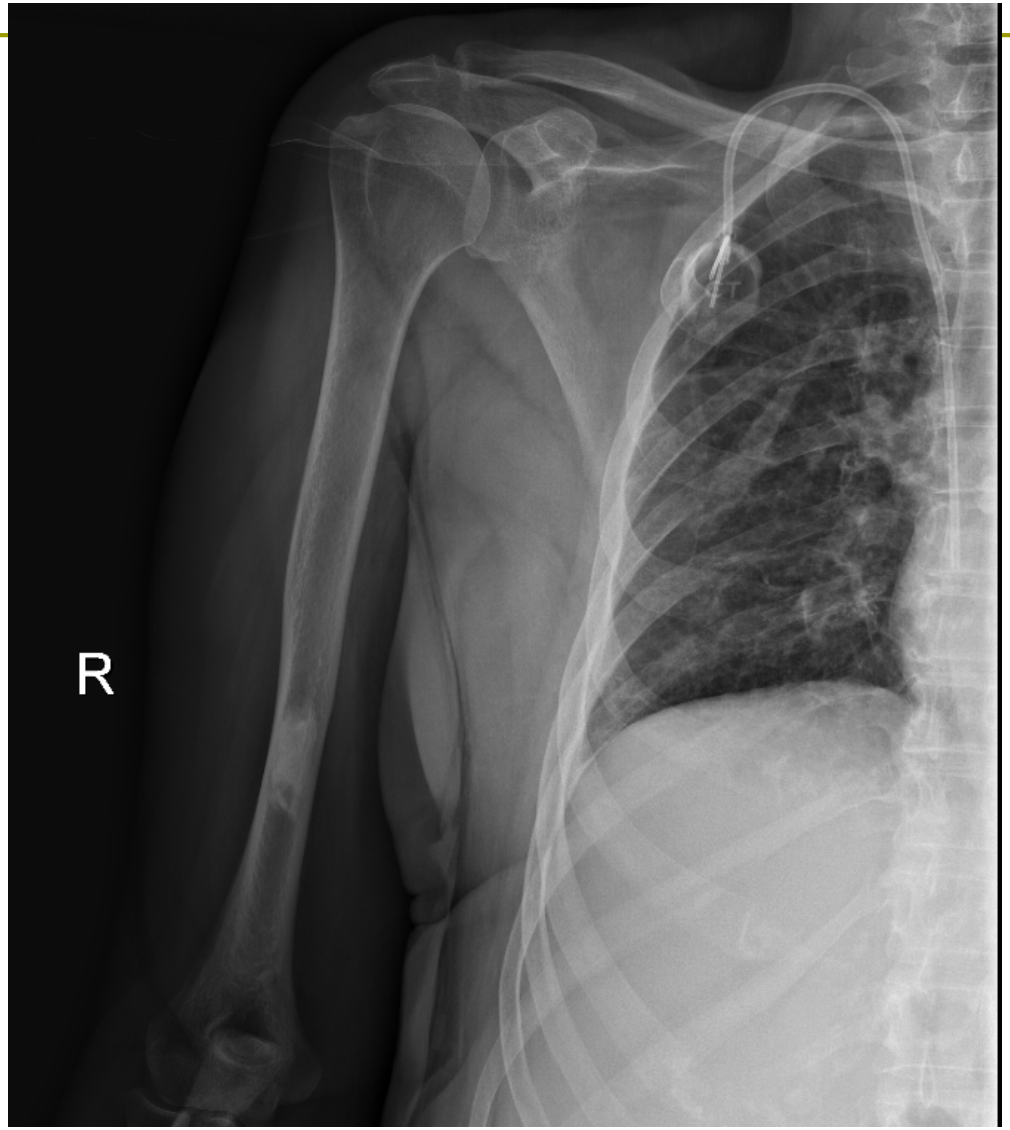
* D'Souza et al, Blood 2012;120:56-62

Treatment Options: "Localized" Disease

- 1 or 2 (3) osteosclerotic lesions without BM involvement
  → **LOCAL RADIATION THERAPY** 40 to 50 Gy
  (>50% NRL responses within months/years and can be curative)



Dispenzieri A et al, Blood 2012 (How I treat); Humeniuk et al, Blood 2013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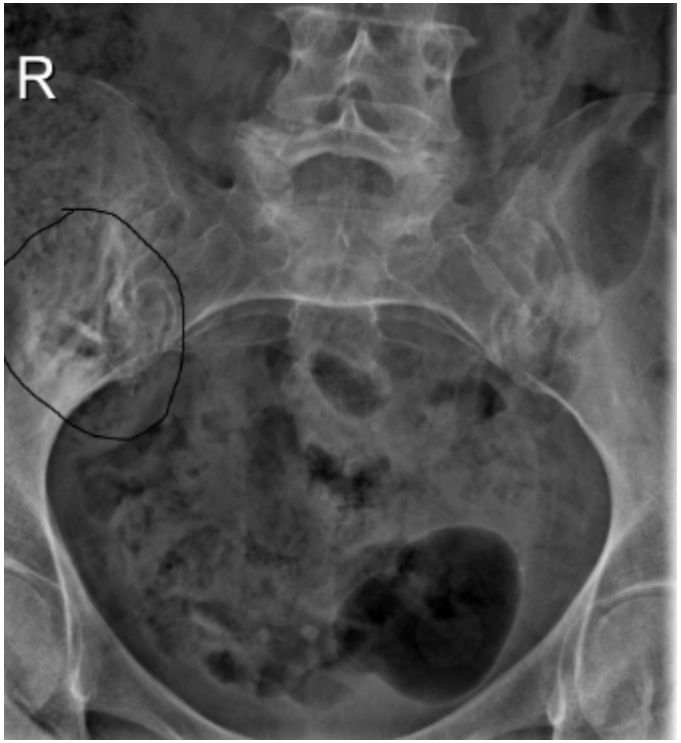
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Treatment Options: Widespread Disease

- Widespread disease (i.e., BM involvement or >2 bone lesions) or progression 3-6 months after completing radiation therapy

  → **SYSTEMIC THERAPY** needed

  +/- RADIATION of a large bone lesion

Regimen	Response Rate
MP	44%
VAD or Cy-based	27%
Prednisone or dexa alone	15%
HDM/SCT in younger patients (Dispenzieri et al, Blood 2004)	Response in 14 of 16 patients, but with significant morbidity (TRM 1/16)

Dispenzieri A. Blood 2012 (How I treat)

ASCT in POEMS Syndrome: First reports

British Journal of Haematology, 2001, **115**, 373–375

SHORT REPORT

Dramatic improvement of POEMS syndrome following autologous haematopoietic cell transplantation

M. Rovira,[1] E. Carreras,[1] J. Bladé,[1] F. Graus,[2] J. Valls,[2] F. Fernández-Avilés[1] and E. Montserrat[1]
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Received 28 March 2001; accepted for publication 15 May 2001

Bone Marrow Transplantation (2001) 28, 305–309

www.nature.com/bmt

Case report

Successful treatment of POEMS syndrome with autologous hematopoietic progenitor cell transplantation

WJ Hogan[1], MQ Lacy[1], GA Wiseman[2], RD Fealey[3], A Dispenzieri[1] and MA Gertz[1]

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Long-term outcomes after ASCT in POEMS syndrome*

- N=59, treated at a single institution (Mayo Clinic, Rochester)
- Median follow-up: 45 months
- Response rate:
  - Hematologic PR or better: 78% (CR 57%)
  - Clinical improvement: 92%
- 5-yr PFS: 75%
  - Most common progression events: Rx > ↑VEGF (rare symptomatic progression)
  - Risk factors for progression: Age ≤ 50 years
    IgG-lambda
    PET-avid lesions at baseline
    Lack of hematologic CR
- 5-yr OS: 94%

* D'Souza et al, Blood 2012;120:56-62

ASCT in POEMS Syndrome Concerns

- Graft failure (10%): PBSC back-up
- Engraftment syndrome (50%): avoid G-CSF
- Pulmonary complications: need for ICU
- TRM: 3%

ASCT in POEMS Syndrome EBMT Long-term Results*

- Study period: 1997-2010 (mFU: 48 mos)
- No. of patients: 127
- Median age: 50 yrs. (range: 26-69)
- Median time from dx to ASCT: 7.5 mos.
- Engraftment syndrome: 23% pts
- Hem RR (PR or better): 69.3% (CR in 48.5%)
- 5yr-PFS: 74%, 5yr-OS: 89%

*Cook G et al (EBMT), Haematologica 2017;102(1):160-7

POEMS and New Drugs

- **Thalidomide/Dex**: anecdotic responses (12 pts), not recommended as first line due to risk of neuropathy
- **Lenalidomide/Dex**: promising responses (>60 pts reported)
- **Bortezomib**: anecdotic responses (5 pts), used alone or in combination
- **Bevacizumab (anti-VEGF-A MoAb)**: anecdotic responses (7 out of 11 pts), two early deaths and two progressions despite normal VEGF

Zagouri et al, Leuk Lymphoma 2014;55:2018-23; Dispenzieri et al, Am J Hematol 2015; 90:952-62.

Lenalidomide* in POEMS Syndrome

- Prospective, open-label, pilot study
- N= 18 patients (13 pre-treated, 5 newly diagnosed but ineligible for HDM)
- Lenalidomide (25 mg/d x 21d) + dexa (40 mg weekly) until progression or intolerance
- Hem RR: 13/18 pts (72%)
- NRL response: 9/18 pts (50%)
- Median FU: 39 months -> 3yr-PFS: 59%
- No discontinuations due to toxicity

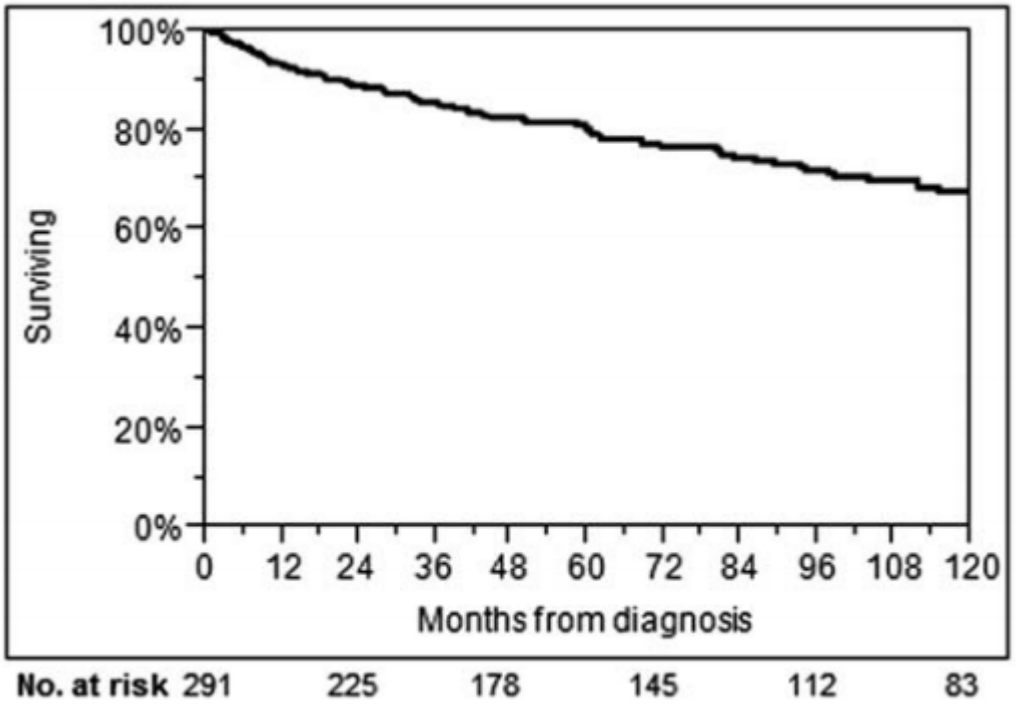
*Nozza et al (Italy), Br J Haematol 2017 (in press)

POEMS Syndrome
Mayo Clinic Long-term Results*

- Study period: 1974-2014
- No. of patients: 291
- Median age: 51 yrs. (range: 19-83)
- Dx after 2003 (n=146):
  - > POEMS features
  - > ASCT (49% vs. 8%)
  - > CR rate (41% vs. 25%)
- OS at 10 yrs: 62%

*Kourelis et al, Am J Hematol 2016;91:585-589

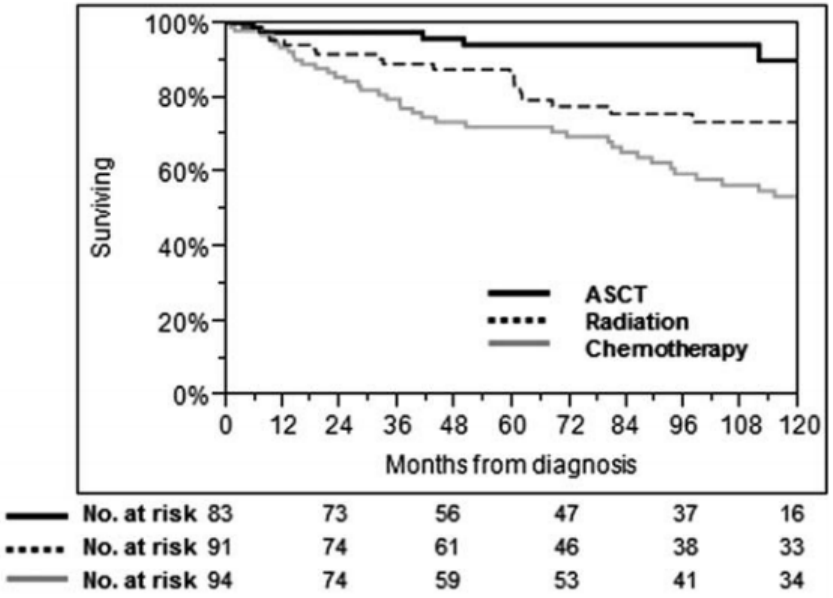
OS for 291 patients with POEMS syndrome*



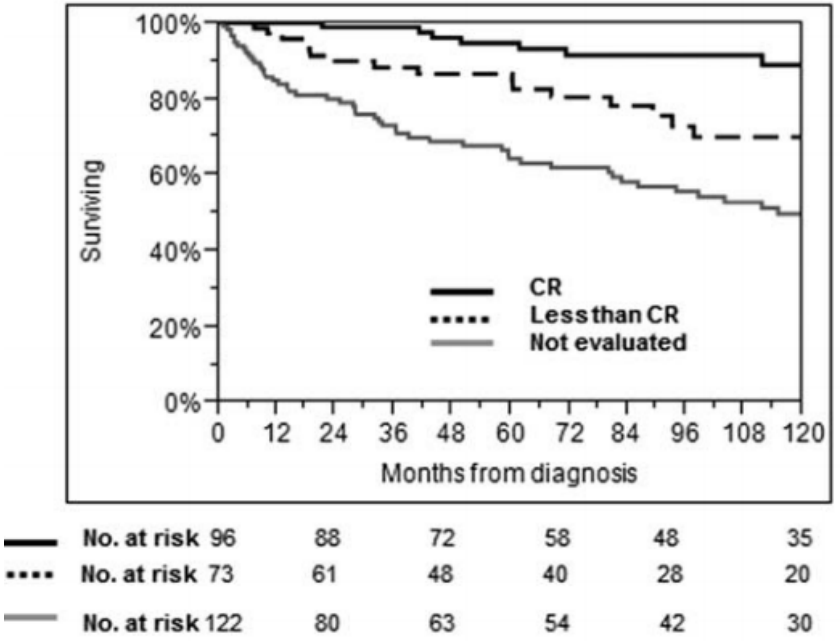
*Kourelis et al, Am J Hematol 2016;91:585-589

OS for 291 patients with POEMS syndrome*

OS according to first line treatment



OS according to depth of hematologic response



*Kourelis et al, Am J Hematol 2016;91:585-589

POEMS syndrome: prognostic features at multivariate analysis*

- Younger age
- Serum albumin > 3.2 g/dL
- CR

*Kourelis et al, Am J Hematol 2016;91:585-589

Daratumumab in POEMS?

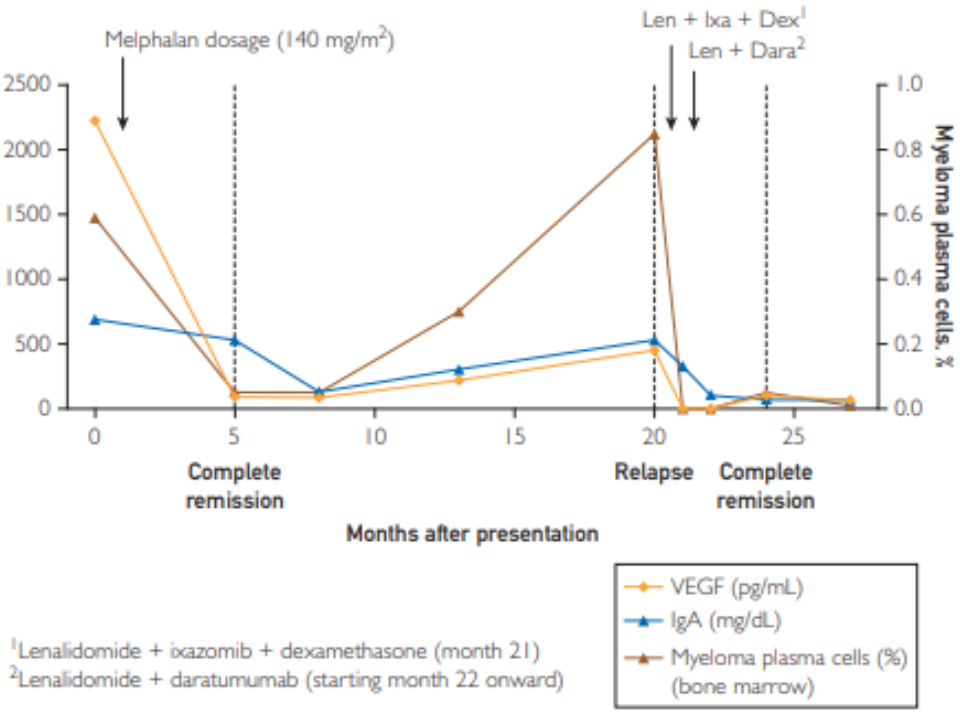


FIGURE. The percentage of myelomatous plasma cells by 8-color flow cytometry, serum levels of vascular endothelial growth factor, and serum levels of β_2-microglobulin shown according to time, treatment modality, and response. VEFG = vascular endothelial growth factor.

Khan M. et al, Mayo Clin Proc 2018 April;93(4):539-547

Muchas gracias