Is there still a role for high dose treatment in AL amyloidosis ?

Yes, but very tiny and not in first line

Arnaud Jaccard

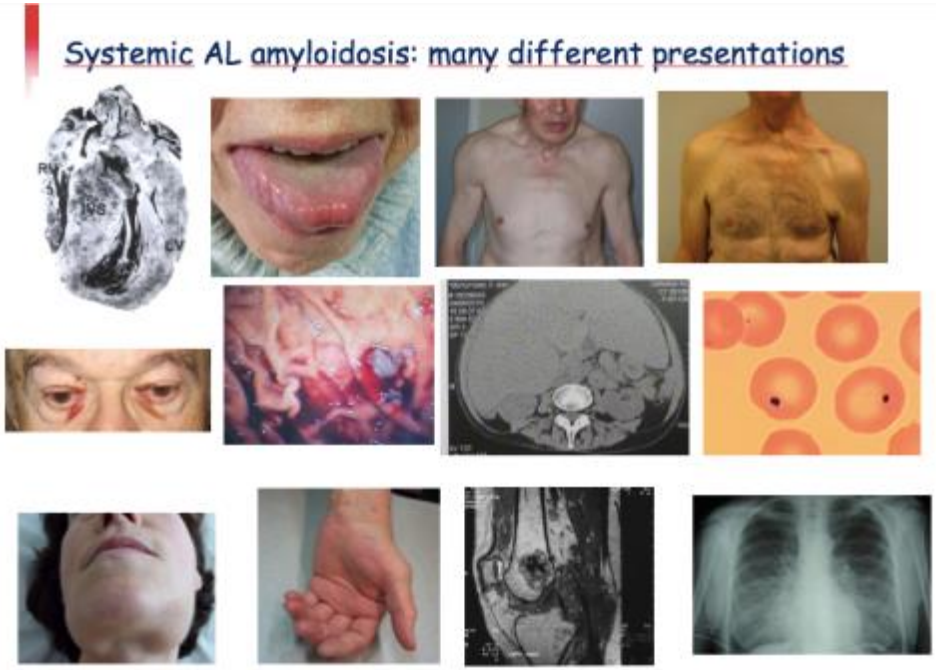
Centre national de référence
Amylose AL
& autres maladies par dépôts d'immunoglobulines monoclonales

CHU Limoges
CHU de Poitiers

AL amyloidosis: usually a "small dangerous B-cell clone" and many organ involved

- MGUS or smoldering myeloma
- Low proliferating index
- 1596 patients with AL amyloidosis seen at the Mayo Clinic : **only 6 evolutions to a symptomatic multiple myeloma** with lytic bone lesions or hypercalcemia (Rajkumar et al, 1994)

- Stress of plasmocytes due to amyloidogenic light chains
  - High sensibility to proteasome inhibitors and dexamethasone
  - Lower relapse rate compared to myeloma

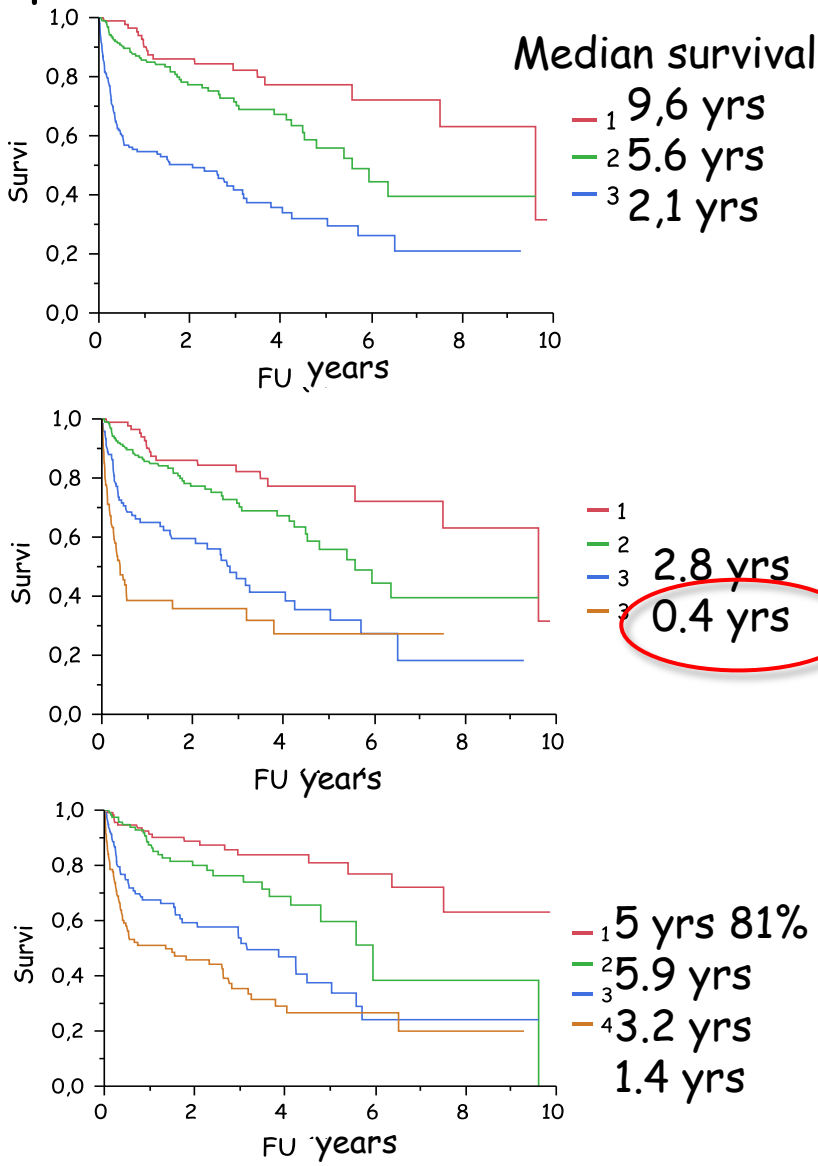


Low bone marrow infiltration by tumoral cells but organs' function frequently impaired particularly heart and kidneys

Prognosis: depending on cardiac biomarkers and dFLC:

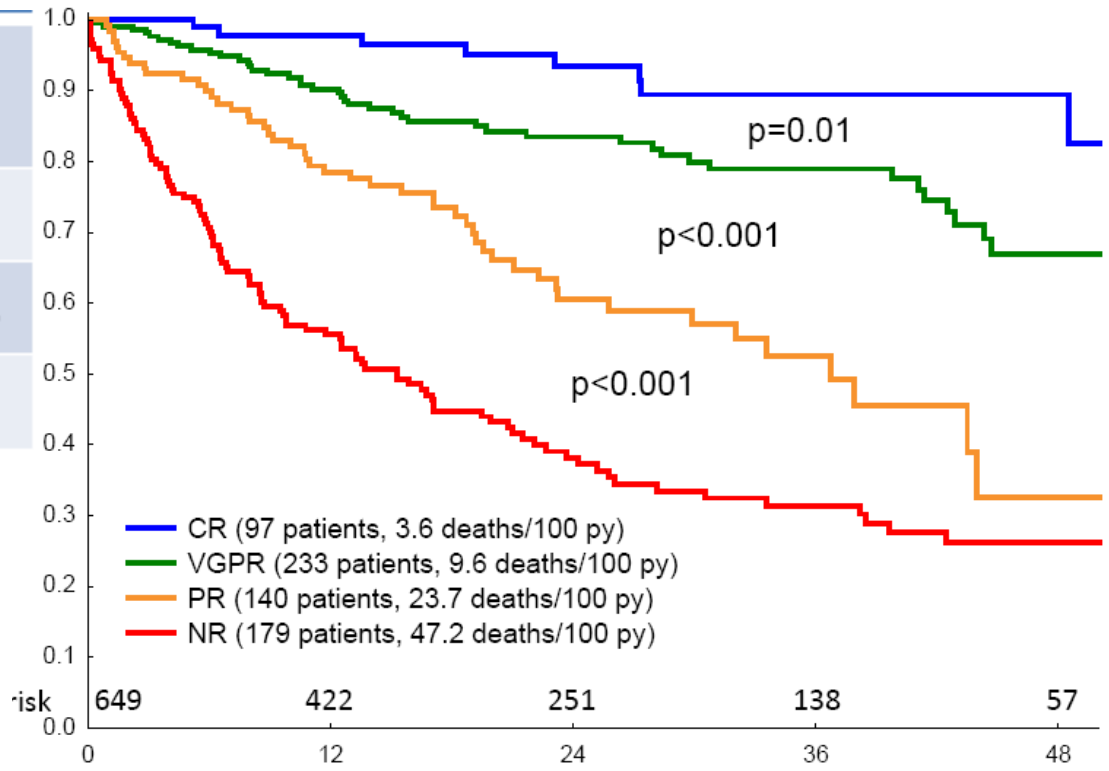
- Classic Mayo Staging (2004):
  - Stage 1 : normal NT-proBNP and troponin
  - Stage 2: only 1 elevated
  - Stage 3: both elevated
- Classic Mayo Staging : European way:
  - Idem for 1 and 2
  - Stage 3a: NT-proBNP < 8500 ng/l
  - Stage 3 b : NT-proBNP > 8500 ng/l
- New Mayo staging (2012)
  - Median NT-proBNT, dFLC, troponin
  - 1, 2, 3 or 4 above the median value

517 patients of the French network



Prognosis: depending on hematologic response

CR	negative s and u IFE normal κ/λ ratio
VGPR	dFLC <40 mg/L
PR	dFLC decrease ≥50%
NR	other



New Criteria for Response to Treatment in Immunoglobulin Light Chain Amyloidosis Based on Free Light Chain Measurement and Cardiac Biomarkers: Impact on Survival Outcomes

Giovanni Palladini, Angela Dispenzieri, Morie A. Gertz, Shaji Kumar, Ashutosh Wechalekar, Philip N. Hawkins, Stefan Schönland, Ute Hegenbart, Raymond Comenzo, Efstathios Kastritis, Meletios A. Dimopoulos, Arnaud Jaccard, Catherine Klersy, and Giampaolo Merlini

VOLUME 30 · NUMBER 36 · DECEMBER 20 2012

JOURNAL OF CLINICAL ONCOLOGY

Treatment of AL amyloidosis

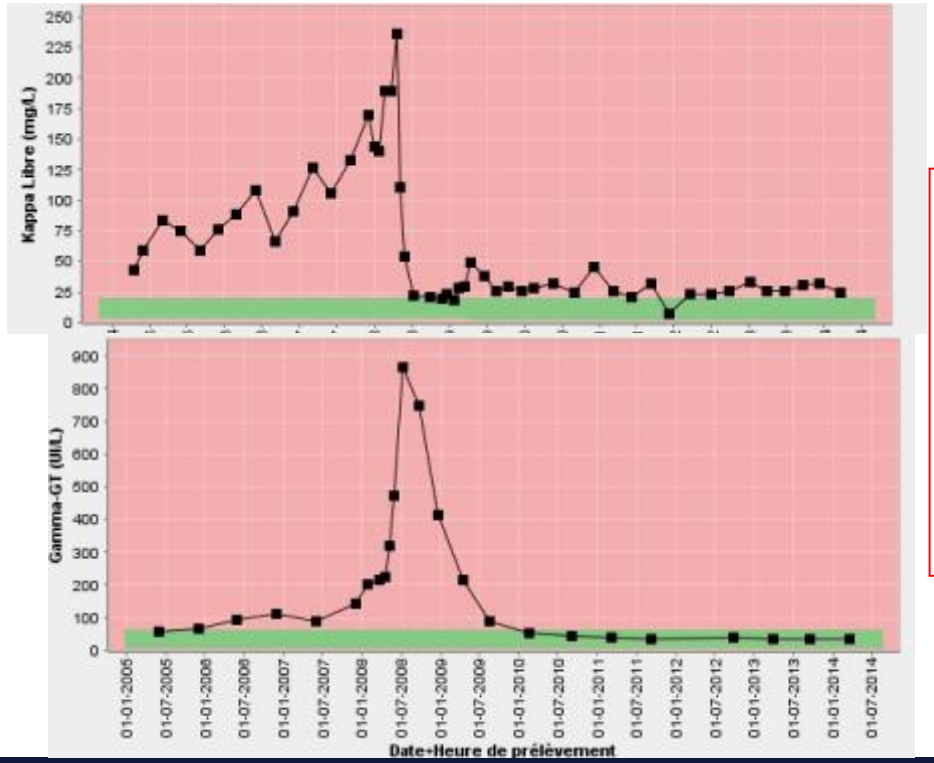
- If the serum level of the amyloidogenic protein decreases, involved organs are getting better, most of the time slowly, with different speed in different organs
- Liver > Kidney > heart > macroglossia

Relapse 3 years after ASCT

Continuous CR 10 years after 5 cycles of bortezomib and dexamethasone

Kappa light chain

Gamma-GT



Chemotherapy is not directly active on amyloidosis deposits

Al amyloidosis therapies, time line and response rates

MP

30%

1965

The NEW ENGLAND JOURNAL of MEDICINE

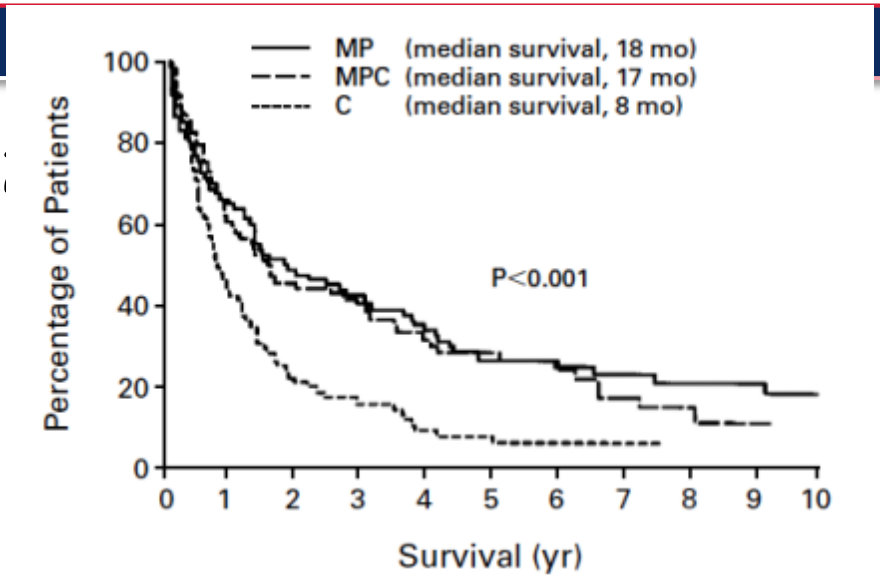
HOME | ARTICLES & MULTIMEDIA | ISSUES | SPECIALTIES & TOPICS | FOR AUTHORS | CME

ORIGINAL ARTICLE

A Trial of Three Regimens for Primary Amyloidosis: Colchicine Alone, Melphalan and Prednisone, and Melphalan, Prednisone, and Colchicine

Robert A. Kyle, M.D., Morie A. Gertz, M.D., Philip R. Greipp, M.D., Thomas E. Witzig, M.D., John A. Lust, M.D., Ph.D., Martha Q. Lacy, M.D., and Terry M. Therneau, Ph.D.

N Engl J Med 1997; 336:1202-1207 | April 24, 1997 | DOI: 10.1056/NEJM199704243361702



ASCT in AL amyloidosis first published case

Haematologica. 1993 Jan-Feb;78(1):68-71.

High-dose therapy and autologous transplantation in amyloidosis-AL.

Majolino I[1], Marcenò R, Pecoraro G, Scimé R, Vasta S, Liberti G, Rizzo A, Indovina A, Caronia F.

⊕ Author information

Abstract

A 53-yr.-old woman with amyloidosis AL was treated with high-dose chemotherapy and autologous stem cell infusion in an attempt to suppress the amyloid secretion. A diagnosis of MGUS had been made six years earlier. During the last year her disease had progressively shifted to a full-blown picture of amyloidosis AL, with renal failure, proteinuria, renal amyloid deposition and plasma cell sheets in the marrow. After an unsuccessful attempt with standard-dose chemotherapy, she received a high-dose regimen of busulphan (14 mg/Kg) and melphalan (40 mg/m2), followed by the infusion of both autologous bone marrow and peripheral blood stem cells. She had full and prompt engraftment, but eight weeks post-graft developed interstitial pneumonitis: CMV was isolated. The patient died while in the intensive care unit. In the literature, this is the first case of amyloidosis AL treated with high-dose therapy and autologous transplantation.

Al amyloidosis therapies, time line and response rates

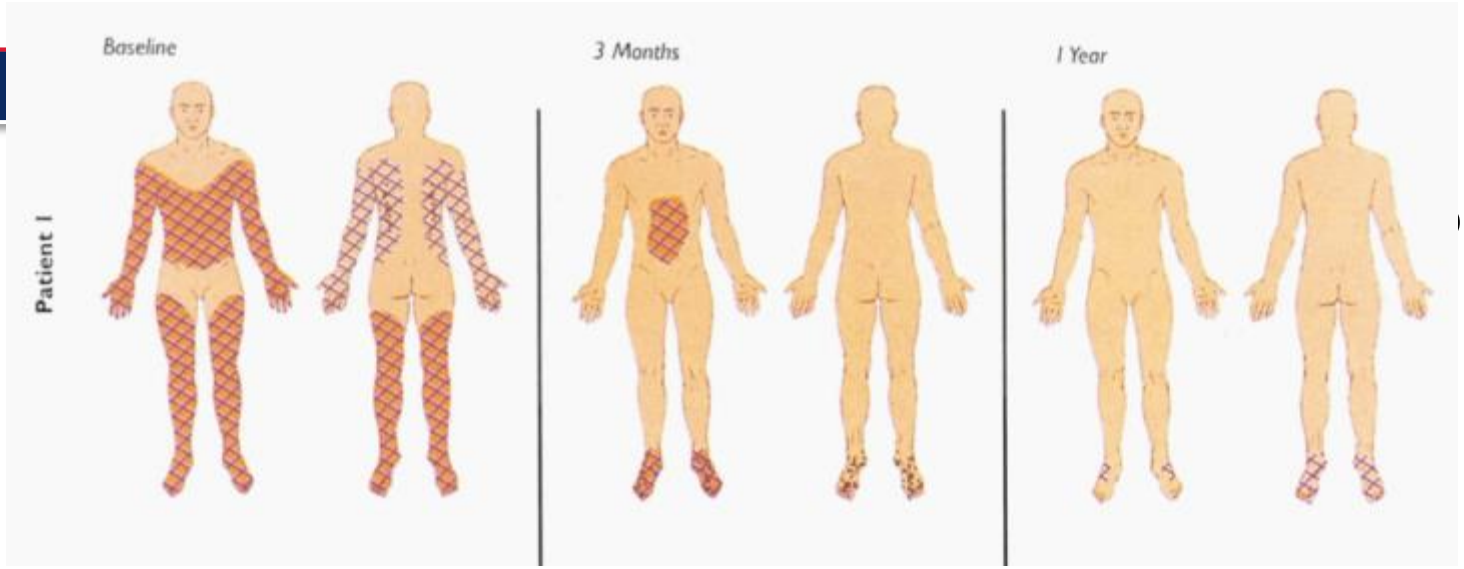
MP	ASCT
30%	65%

Dose-Intensive Melphalan With Blood Stem Cell Support for the Treatment of AL Amyloidosis: One-Year Follow-up in Five Patients

By Raymond L. Comenzo, Evan Vosburgh, Robert W. Simms, Peter Bergethon, Diane Sarnacki, Kathleen Finn, Simon Dubrey, Douglas V. Faller, Daniel G. Wright, Rodney H. Falk, and Martha Skinner

Blood, Vol 88, No 7 (October 1), 1996: pp 2801-2806

1965 1996



But TRM ?

British Journal of Haematology, 1998, 101, 766–769

Prognostic factors for survival and response after high-dose therapy and autologous stem cell transplantation in systemic AL amyloidosis: a report on 21 patients

Philippe Moreau, Véronique Leblond, Priscille Bourquelot, Thierry Facon, Anne Huynh, Denis Caillot, Olivier Hermine, Michel Attal, Mohamed Hamidou, Gérard Nedellec, Augustin Ferrant, Bruno Audhuy, Régis Bataille, Noël Milpied and Jean-Luc Harousseau *Department of Haematology, CHU Hôtel-Dieu, Nantes, France*

TRM before 1 month post ASCT:
43% of patients

Toxicity

Nine toxic deaths were observed within the first month following transplantation from multi-organ failure (acute renal failure + oedema with pleural and pericardial effusions + hepatic dysfunction; $n = 5$), multi-organ failure + severe bleeding ($n = 1$), multi-organ failure + sudden death attributed to cardiac arrhythmia ($n = 1$) and sudden death due to cardiac arrhythmia ($n = 2$). With a median follow-up

TRM also for stem cell collection

Biol Blood Marrow Transplant 24 (2018) 815–819

Adverse Prognostic Factors for Morbidity and Mortality During Peripheral Blood Stem Cell Mobilization in Patients with Light Chain Amyloidosis

Jason C. Yeh [1,*], Brandon R. Shank [1], Denái R. Milton [2], Muzaffar H. Qazilbash [3]

101 patients

Table 2
Incidence of Adverse Events Included in Composite Endpoint During PBSC Mobilization

Adverse Event	Value
Cardiac event, n (%)	7 (7)
Thromboembolic event, n (%)	5 (5)
Bleeding event, n (%)	3 (3)
Hospitalization, n (%)	14 (14)
Weight gain >2% necessitating diuretic intervention, n (%)	30 (30)
Mortality, n (%)	4 (4)

A total of 63 adverse events occurred in 41 patients.

Why to choose ASCT instead of conventional treatment ?

- Better response rate
- Better PFS
- Better survival

Al amyloidosis therapies, time line and response rates

MP 30%

ASCT 65%

MDEX 67%

CLINICAL OBSERVATIONS, INTERVENTIONS, AND THERAPEUTIC TRIALS

Brief report

Association of melphalan and high-dose dexamethasone is effective and well tolerated in patients with AL (primary) amyloidosis who are ineligible for stem cell transplantation

Giovanni Palladini, Vittorio Perfetti, Laura Obici, Riccardo Caccialanza, Alessandra Semino, Fausto Adami, Giobatta Cavallero, Roberto Rustichelli, Giovambattista Virga, and Giampaolo Merlini

BLOOD, 15 APRIL 2004 • VOLUME 103, NUMBER 8

Thirty-one patients (67%) obtained a hematologic response, and 15 (33%) of these patients achieved complete hematologic remission. The median time to response was 4.5 months (range, 2.3-10.1

Forty-six patients referred between December 1999 and October 2002

1965 1995 2000 2003 2006 2012 2016

Al amyloidosis therapies, time line and response rates

MP 30%

ASCT 68%

MDEX 67%

1965 1995 2000

ORIGINAL ARTICLE

High-Dose Melphalan versus Melphalan plus Dexamethasone for AL Amyloidosis

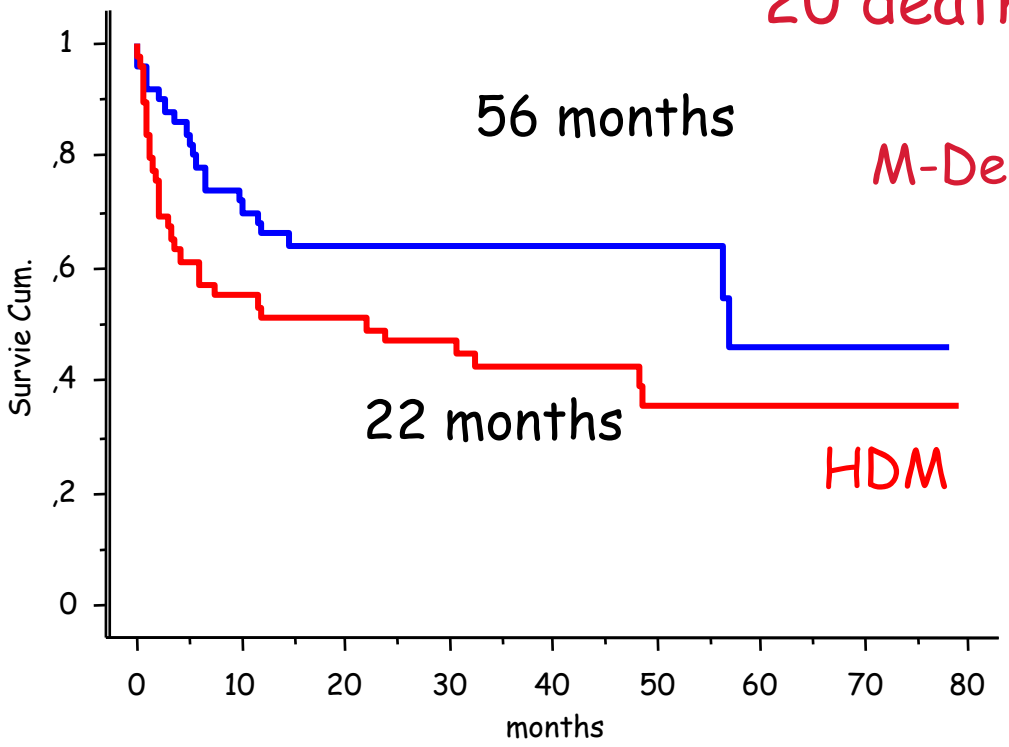
Arnaud Jaccard, M.D., Philippe Moreau, M.D., Veronique Leblond, M.D., Xavier Leleu, M.D., Lotfi Benboubker, M.D., Ph.D., Olivier Hermine, M.D., Ph.D., Christian Recher, M.D., Bouchra Asli, M.D., Bruno Lioure, M.D., Bruno Royer, M.D., Fabrice Jardin, M.D., Ph.D., Frank Bridoux, M.D., Ph.D., Bernard Grosbois, M.D., Jérome Jaubert, M.D., Jean-Charles Piette, M.D., Pierre Ronco, M.D., Ph.D., Fabrice Quet, M.Sc., Michel Cogne, M.D., Ph.D., and Jean-Paul Fermand, M.D., for the Myélome Autogreffe (MAG) and Intergroupe Francophone du Myélome (IFM) Intergroup*

N Engl J Med 2007;357:1083-93.

Group Assigned to Melphalan plus Dexamethasone (N=38)	Group Ass to High-D Melphalan (N=27)
12	11
14	7
26 (68)	18 (67)
26/50 (52)	18/50 (36)

Survival according to arm

Intent to treat



20 deaths

56 months

M-Dex

22 months

HDM

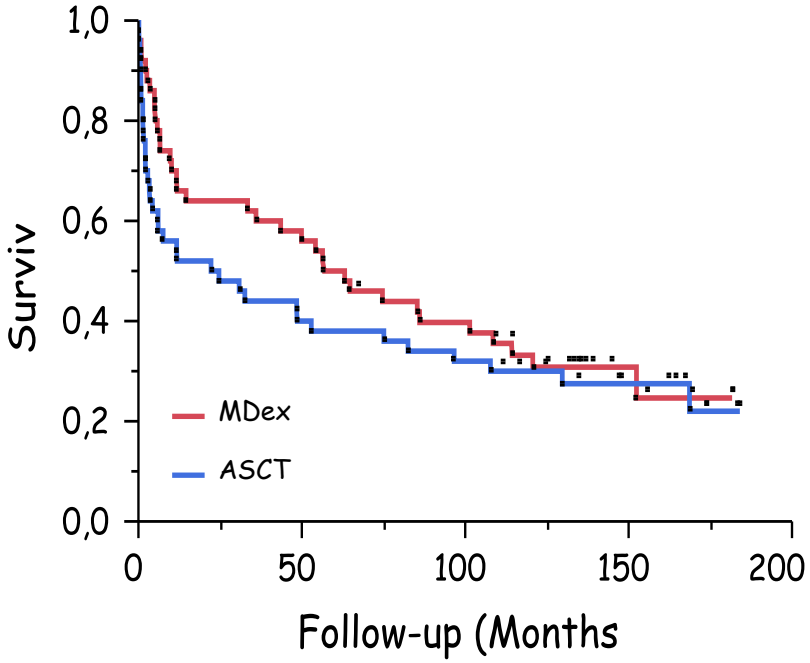
31 deaths

Chi-2	DDL	P
3,906	1	**0,0481**

Any advantage for ASCT 10 years after?

Survival, April 2016

Follow-up for living patients: 11.8 years

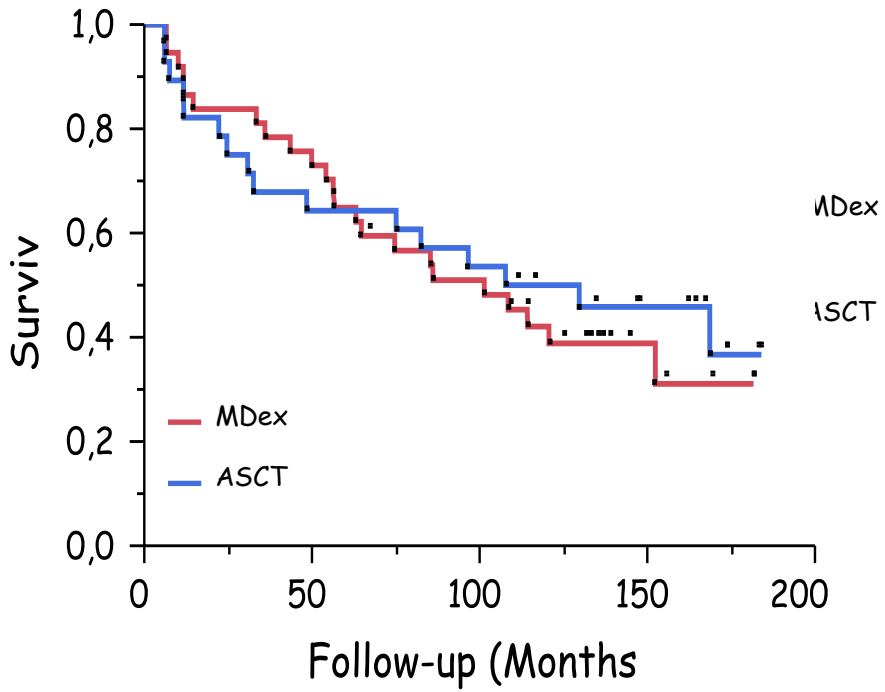


Mdex : 15 alive patients

ASCT: 13 alive patients

Any advantage for ASCT 10 years after?

Landmark analysis, April 2016



Pts surviving 6 months who received their allotted treatment

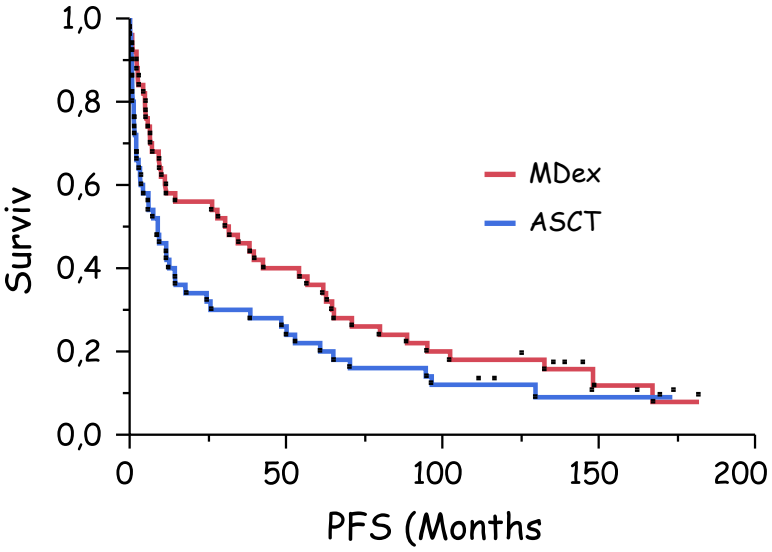
HDM (n = 29)

3 M-Dex (n = 37)

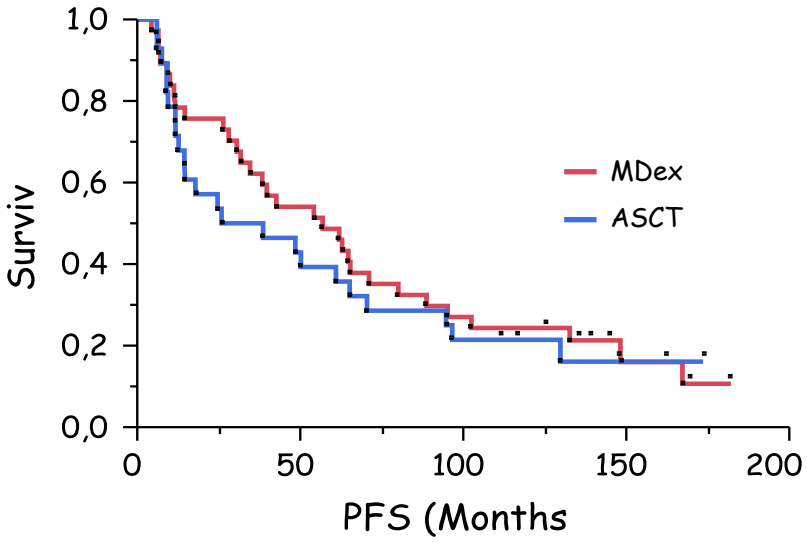
TRM: 0%
Feasibility: 100%

Any advantage for ASCT 10 years after? PFS

Whole cohort



Landmark analysis



Patients who have not received second line treatment:

ASCT : 5 M-Dex : 6

Myelodysplasia:

ASCT : 1 M-Dex : 2

bjh correspondence

Disease-free survival following high dose or standard dose therapy in patients with amyloidosis

sept 2015

Patrick J. Kiel[1]
Anne O. Trueg[1]
Meagan Ferguson[1]
Merrill Benson[2]
Rafat Abonour[2]
[1]Department of Pharmacy, Indiana University Health Simon Cancer Center, and [2]Indiana University School of Medicine, Indianapolis, IN, USA.

Table I. Amyloid according to the organ involved.

Organ	High-dose, *n* (%) (*N* = 43)	Standard dose, *n* (%) (*N* = 25)
Renal	32 (76·7)	12 (48)
Gastrointestinal	2 (4·7)	(0)
Hepatic	3 (7)	1 (4)
Cardiac	3 (7)	10 (40)
Other	3 (7)	2 (8)

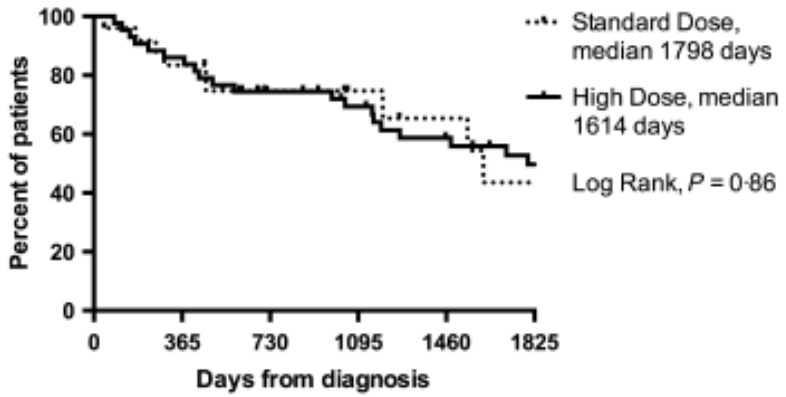


Figure 1. Disease-free survival.

Why to chose ASCT instead of conventional treatment

- Better response rate : no
- Better PFS: no
- Better survival no
  - Higher TRM

Nephrol Dial Transplant (2016) 31: 1284–1289
doi: 10.1093/ndt/gfv328
Advance Access publication 30 November 2015

ndt
Nephrology Dialysis Transplantation

Original Article

The impact of dialysis on the survival of patients with immunoglobulin light chain (AL) amyloidosis undergoing autologous stem cell transplantation

Nelson Leung[1,2], Shaji K. Kumar[1], Siobhan V. Glavey[1], Angela Dispenzieri[1], Martha Q. Lacy[1], Francis K. Buadi[1], Suzanne R. Hayman[1], David Dingli[1], Prashant Kapoor[1], Steven R. Zeldenrust[1], Stephen J. Russell[1], John A. Lust[1], William J. Hogan[1], S. Vincent Rajkumar[1], Dennis A. Gastineau[1], Taxiarchis V. Kourelis[1], Yi Lin[1], Wilson I. Gonsalves[1], Ronald S. Go[1] and Morie A. Gertz[1]

Nephrol Dial Transplant (2016) 31: 1199–1202
doi: 10.1093/ndt/gfv460
Advance Access publication 1 February 2016

Is there still a place for autologous stem cell transplantation in systemic AL amyloidosis with severe renal disease?

Frank Bridoux[1], Vincent Javaugue[1], Jean Paul Fermand[2] and Arnaud Jaccard[3]

Al amyloidosis therapies, time line and response rates

haematologica/the hematology journal | 2007; 92(10) | 1351 |

Original Article

Treatment of light chain (AL) amyloidosis with the combination of bortezomib and dexamethasone

Efstathios Kastritis, Athanasios Anagnostopoulos, Maria Roussou, Savvas Toumanidis, Constantinos Pamboukas, Magdalini Migkou, Anna Tassidou, Irini Xilouri, Sossana Delibasi, Erasmia Psimenou, Sofia Mellou, Evangelos Terpos, John Nanas, Meletios A. Dimopoulos

. Thus 15 (94%) of 16 evaluable patients had a hematologic response and seven (44%) achieved a hematologic CR.[35]

Bortezomib
CyborD/VCD
80/94%

● ● ● CLINICAL TRIALS

Comment on Mikhael et al, page 4391, and on Venner et al, page 4387

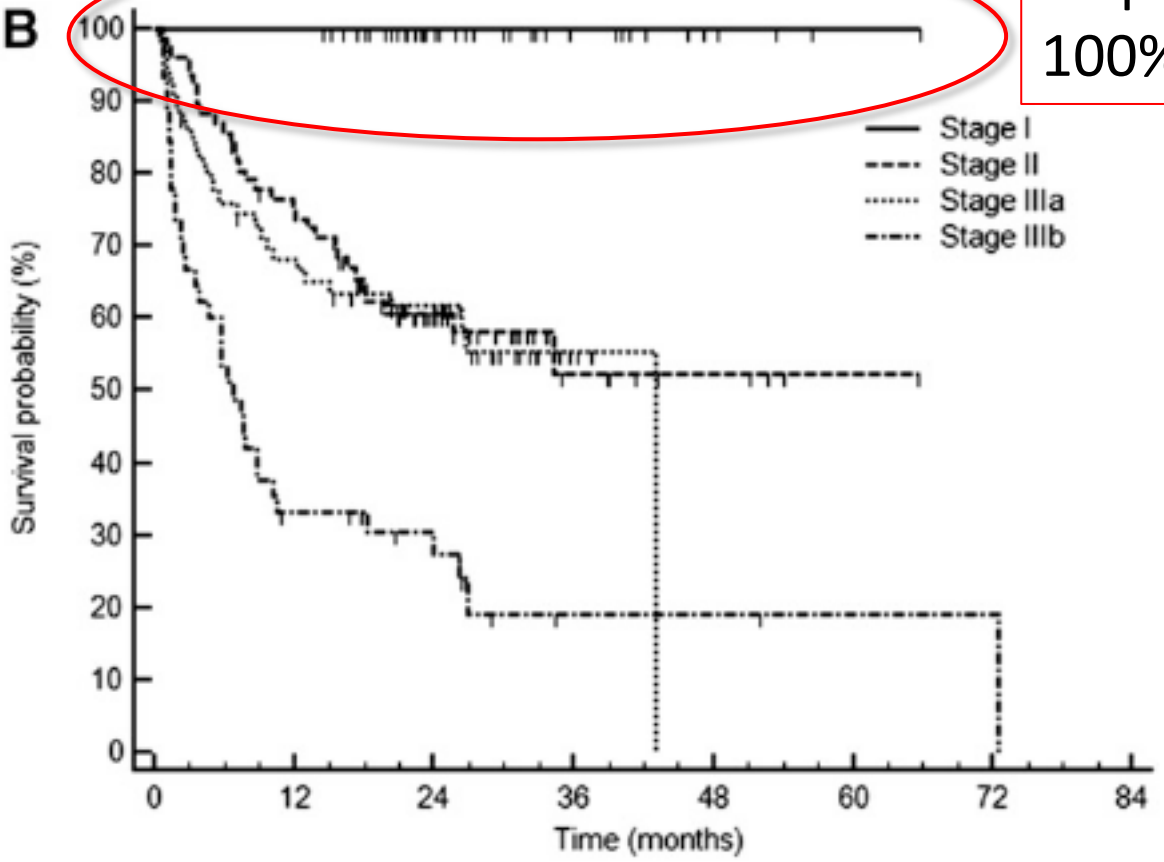
CyBorD: stellar response rates in AL amyloidosis

blood 10 MAY 2012 | VOLUME 119, NUMBER 19

Giampaolo Merlini PAVIA UNIVERSITY HOSPITAL SAN MATTEO

A European collaborative study of cyclophosphamide, bortezomib, and dexamethasone in upfront treatment of systemic AL amyloidosis

Giovanni Palladini,[1] Sajitha Sachchithanantham,[2] Paolo Milani,[1] Julian Gillmore,[2] Andrea Foli,[1] Helen Lachmann,[2] Marco Basset,[1] Philip Hawkins,[2] Giampaolo Merlini,[1] and Ashutosh D. Wechalekar[2]



30 patients
100% survival

Why to chose ASCT instead of conventional treatment

- Better response rate : no, lower than with new regimens
- Better PFS: no
- Better survival no

Why so many papers argue for ASCT's superiority ?

High-dose therapy for amyloidosis: the end of the beginning?

The data from the Mayo Clinic and Boston University are impressive enough to make a prospective, randomized study of high- versus conventional-dose therapy in amyloidosis scientifically unattractive and practically impossible.

BLOOD, 15 MAY 2004 • V

- Usually not in intent to treat
- Often in very specialized centers

- Selection +++

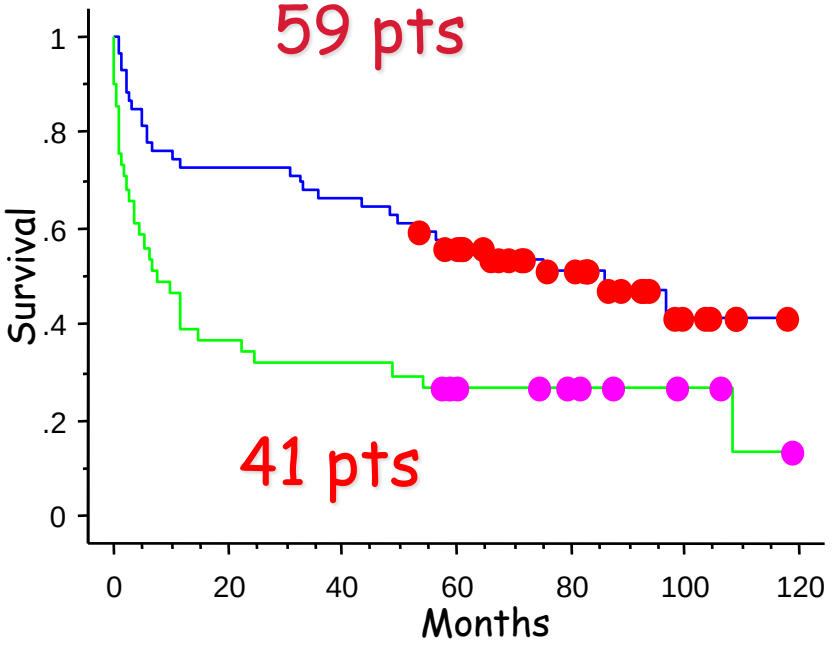
High and low risk subgroups (Mayo clinic criteria), whatever treatment

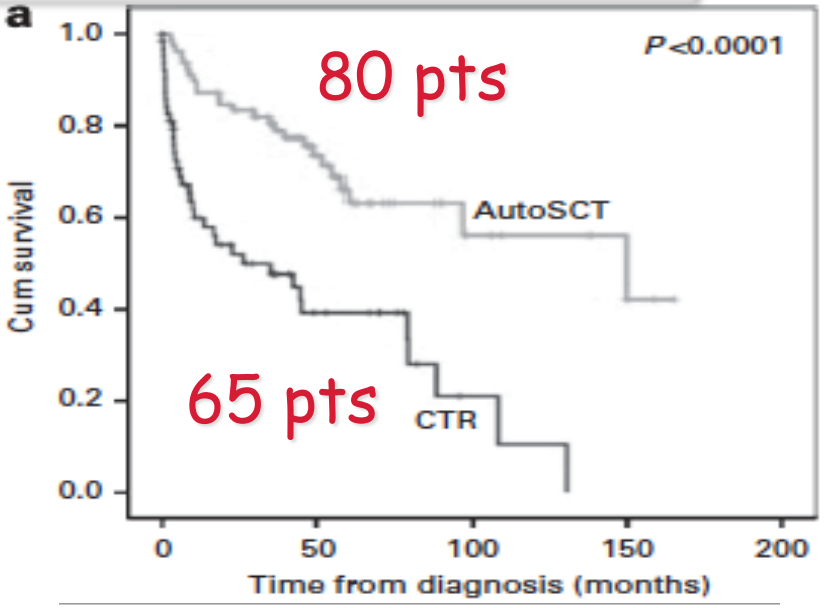
ORIGINAL ARTICLE Bone Marrow Transplantation (2014) 49, 1036–1041

Auto-SCT improves survival in systemic light chain amyloidosis: a retrospective analysis with 14-year follow-up

S Parmar[1], P Kongtim[1], R Champlin[1], Y Dinh[1], Y Elgharably[1], M Wang[2], Q Bashir[1], JJ Shah[2], N Shah[1], U Popat[1], SA Giralt[3], RZ Orlowski[2] and MH Qazilbash[1]

5 years survival : 60 % vs 30 % 68 % vs 38 %





Low risk : interventricular septal thickness ≤15 mm, cardiac ejection fraction > 55 %, serum creatinine ≤ 2.0 mg/dL, bilirubin ≤ 2.0 mg/dL)

Table 1. Patient characteristics

	Auto-SCT (n = 80)	*CTR (n = 65)*	*P-value*
Age, years	56 (34–74)	61 (33–87)	0.0001
Race (Caucasian)	50 (62%)	46 (71%)	0.05
Gender (Female)	32 (40%)	32 (49%)	0.3
Organ involvement ⩾2	26 (33%)	33 (51%)	0.03
Cardiac involvement	18 (23%)	31 (48%)	0.0001
Renal involvement	55 (69%)	43 (66%)	0.8
Serum Cr ⩾2.5 mg/dL	8 (10%)	15 (23%)	0.04
BM plasma cells >10%	29 (36%)	36 (55%)	0.006
Hb ⩽10 g/dL	6 (7.5%)	13 (20%)	0.04
LVEF < 50%	2 (2.5%)	10 (15%)	0.03

Biol Blood Marrow Transplant 23 (2017) 1473–1477

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Outcomes from Autologous Hematopoietic Cell Transplantation versus Chemotherapy Alone for the Management of Light Chain Amyloidosis

Oluchi Oke [1], Tarsheen Sethi [2], Stacey Goodman [2], Sharon Phillips [3], Ilka Decker [1], Samuel Rubinstein [1], Beatrice Concepcion [4], Sarah Horst [5], Madan Jagasia [2], Adetola Kassim [2], Shelton L. Harrell [2], Anthony Langone [4], Daniel Lenihan [6], Kyle T. Rawling [2], David Slosky [6], Robert Frank Cornell [2,*]

	ASCT	CT
BNP: pg/ml	192	501

In conclusion, although the efficacy of AHCT as a first-line therapy has been controversial in previous studies, our findings support AHCT as an effective treatment for AL amyloidosis.

This study showed increased PFS, depth of response, and overall survival in patients who underwent AHCT versus chemotherapy alone.

In this study, 100 day TRM was 7%.

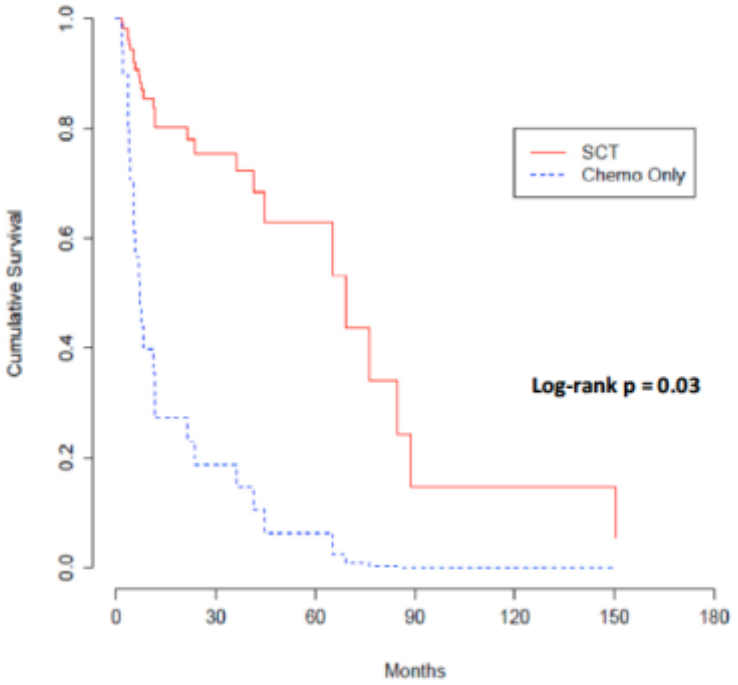
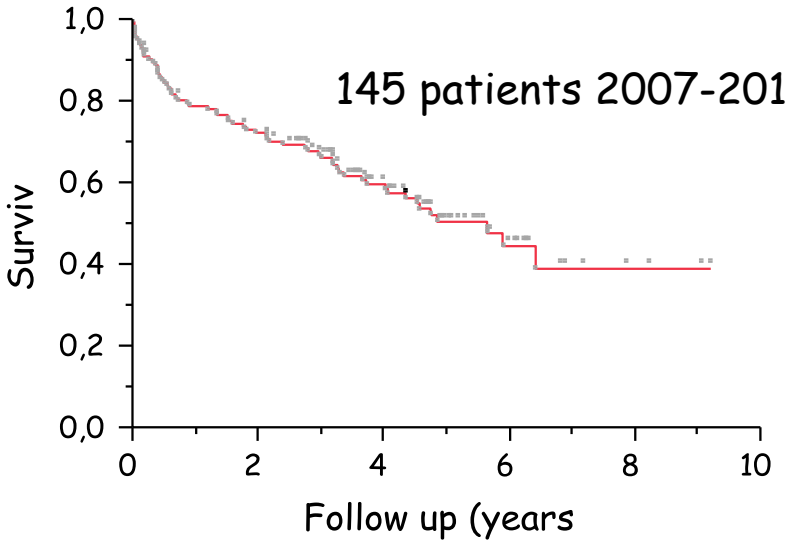
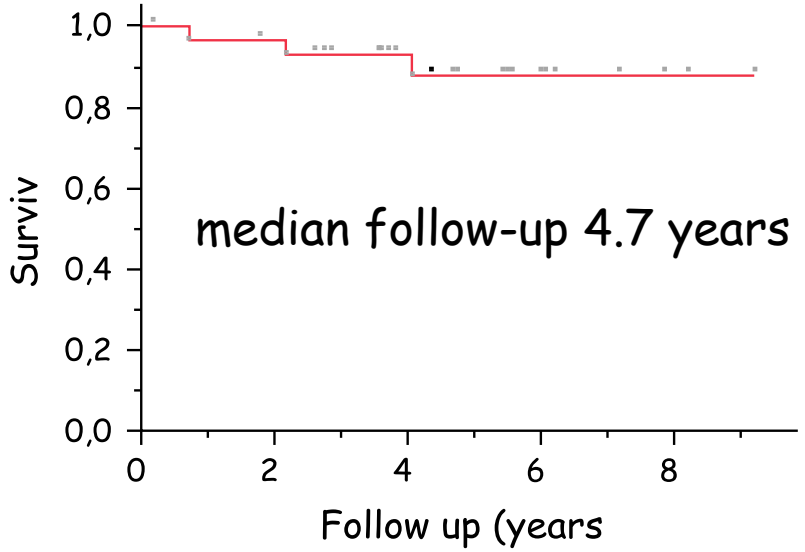


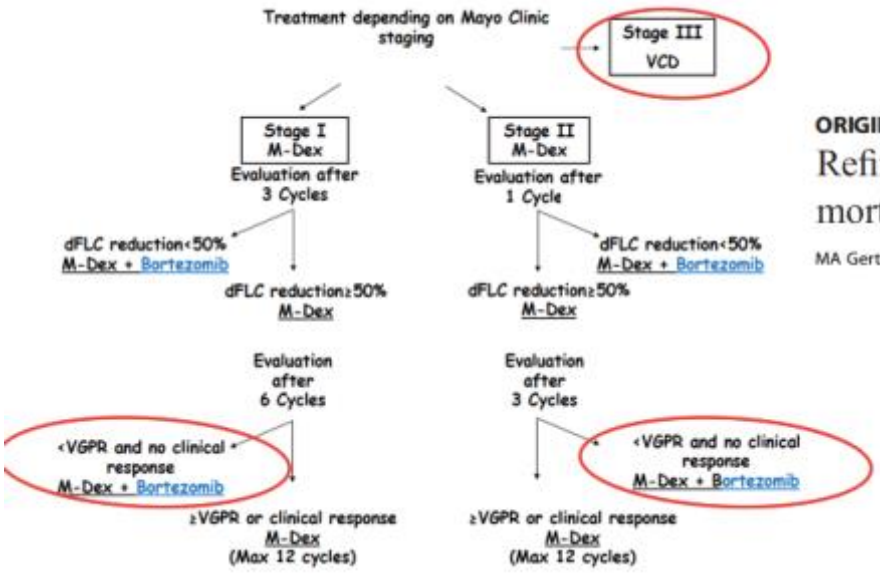
Figure 1. Overall survival in patients with AL amyloidosis treated with AHCT or chemotherapy alone.

Survival for very good patients with conventional treatment



30 patients/145 = 20.6%





ORIGINAL ARTICLE

Refinement in patient selection to reduce treatment-related mortality from autologous stem cell transplantation in amyloidosis

MA Gertz[1], MQ Lacy[1], A Dispenzieri[1,2,3], SK Kumar[1], D Dingli[1,3], N Leung[3,4], WJ Hogan[1], FK Buadi[1] and SR Hayman[1]

BMT 2013; 48:557-61

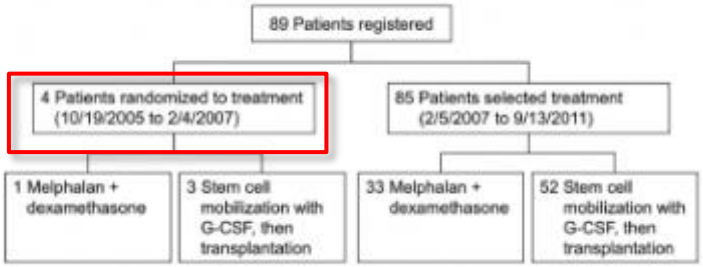
Age<70 NTproBNP<5000ng/L;
cTnT<0,06µg/L Creat≤150µmol/L
Org invol<3 BNP<500ng/L
hs-cTnT<0,1 µg/L cTnI<0,2 µg/L

And the M-Dex vs ASCT done in the Mayo Clinic ?

Stem Cell Transplantation Compared With Melphalan Plus Dexamethasone in the Treatment of Immunoglobulin Light Chain Amyloidosis

Cancer. 2016 July 15; 122(14): 2197–2205.

Morie A. Gertz, MD, MACP, Martha Q. Lacy, MD, Angela Dispenzieri, MD, Francis K. Buadi, MD, David Dingli, MD, PhD, Suzanne R. Hayman, MD, Shaji Kumar, MD, Nelson Leung, MD, John Lust, MD, S. Vincent Rajkumar, MD, Stephen J. Russell, MD, PhD, Vera J. Suman, PhD, Jennifer G. Le-Rademacher, PhD, and **William J. Hogan, MB, BCh**



Characteristic	Melphalan + Dexamethasone (n=34)	Autologous Stem Cell Transplantation (n=55)
κ/λ ratio	0.07 (0.02-0.15)	0.15 (0.04-0.96)
Free light chain assay, median (IQR), mg/dL		
κ free light chain	1.42 (0.99-1.98)	1.28 (0.90-2.72)
λ free light chain	28.25 (8.79-44.8)	8.41 (2.32-18.6)

0 1 2 3 4 5 6 7 8

Time, y

Kidney	18 (52.9)	36 (65.5)
Heart	14 (41.2)	8 (14.6)

Why M140 is so bad in amyloidosis

ORIGINAL ARTICLE

Bone Marrow Transplantation (2017) **52,** 1126–1132

Revisiting conditioning dose in newly diagnosed light chain amyloidosis undergoing frontline autologous stem cell transplant: impact on response and survival

N Tandon[1,4], E Muchtar[1,4], S Sidana[1], A Dispenzieri[1], MQ Lacy[1], D Dingli[1], FK Buadi[1], SR Hayman[1], R Chakraborty[1,2], WJ Hogan[1], W Gonsalves[1], R Warsame[1], TV Kourelis[1], N Leung[1,3], P Kapoor[1], SK Kumar[1] and MA Gertz[1]

In summary, this study demonstrated that AL amyloidosis patients treated with ASCT in first line have inferior response and shorter survival with the use of reduced-dose melphalan.

And not in myeloma ?

Haematologica 2018
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Melphalan 140 mg/m² or 200 mg/m² for autologous transplantation in myeloma: results from the Collaboration to Collect Autologous Transplant Outcomes in Lymphoma and Myeloma (CALM) study. A report by the EBMT Chronic Malignancies Working Party

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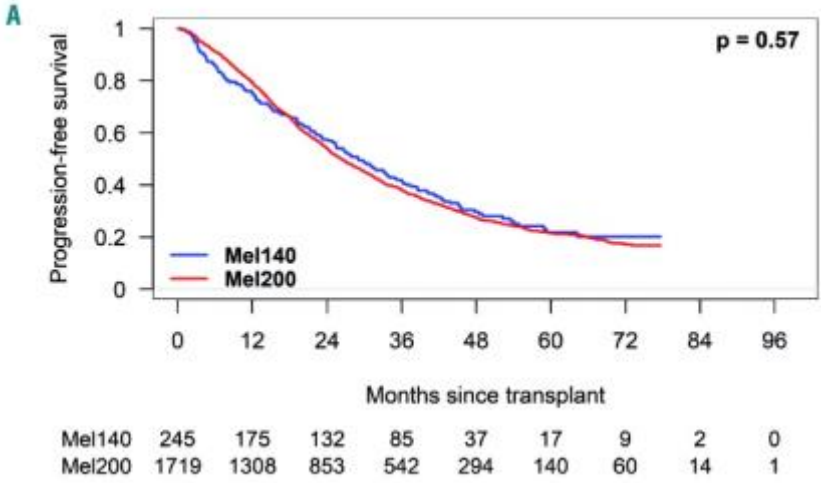

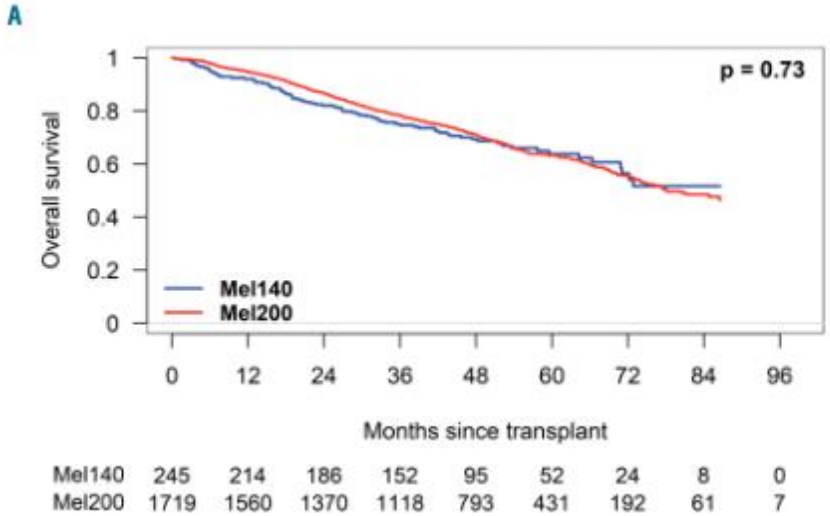

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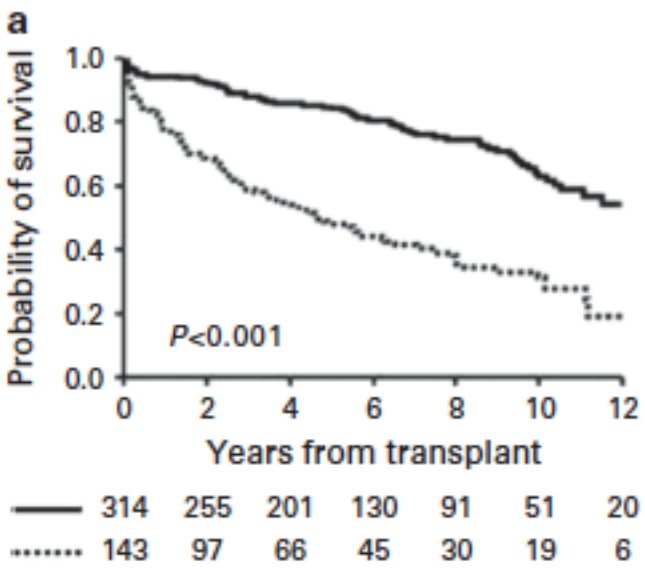

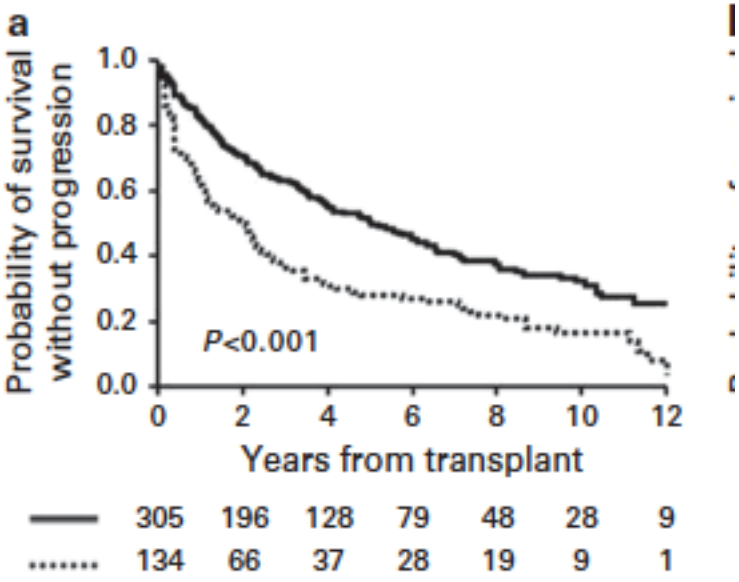

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Table 1. Baseline characteristics of the entire cohort and by the conditioning-intensity groups (clinical)

	Entire cohort (n = 457)	*Full-intensity group (n = 314)*	*Reduced-intensity group (n = 143)*	*P-value*
Age, years median (IQR)	58 (52–64)	57 (51–62)	60 (53–67)	< **0.001**
Age ⩾65 years, *N* (%)	104 (23%)	53 (17%)	51 (36%)	< **0.001**
Male sex, *N* (%)	270 (59%)	183 (58%)	87 (61%)	0.6
PS, Karnofsky score, median (IQR; *n* = 380)	80 (80–90)	80 (80–90)	80 (70–80)	< **0.001**
Karnofsky ⩾80, *N* (%)	294 (77%)	228 (85%)	66 (57%)	< **0.001**
Organ involved, N (%)				
>1 Organs	245 (54%)	147 (47%)	98 (69%)	< **0.001**
Cardiac	254 (56%)	143 (46%)	111 (78%)	< **0.001**
Renal	304 (67%)	205 (65%)	99 (69%)	0.4
Hepatic	64 (14%)	38 (12%)	26 (18%)	0.08
GI	63 (14%)	45 (14%)	18 (13%)	0.61
Neurological	77 (17%)	52 (17%)	25 (17%)	0.8
2004 Mayo stage, N (%; n = 352)				
I/II	297 (84%)	232 (90%)	65 (69%)	< **0.001**
III	55 (16%)	26 (10%)	29 (31%)	
2012 Mayo stage, N (%; n = 373)				
I/II	323 (87%)	245 (91%)	78 (76%)	< **0.001**
III/IV	50 (13%)	25 (9%)	25 (24%)	

Abbreviations: GI = gastrointestinal; IQR = interquartile range; PS = performance status. Bold indicates statistical significance at $P < 0.05$.

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Table 2. Baseline characteristics of the entire cohort and by the conditioning-intensity groups (laboratory)

	Entire cohort (n = 457)	*Full-intensity group (n = 314)*	*Reduced-intensity group (n = 143)*	*P-value*
Lambda-restricted, *N* (%)	346 (76%)	236 (75%)	110 (77%)	0.68
BMPCs, median (IQR)	8 (5–12)	8 (5–11)	10 (5–15)	0.12
⩾10% BMPCs, *N* (%)	200 (44%)	127 (40%)	73 (52%)	**0.02**
dFLC, mg/dL, Median (IQR; *n* = 414)	18 (7–54)	14 (6–44)	27 (10–70)	**0.002**
dFLC ⩾ 18 mg/dL, *N* (%)	205 (50%)	132 (45%)	73 (60%)	**0.004**
NT-proBNP, pg/mL, median (IQR; *n* = 353)	473 (149–1802)	351 (122–1137)	1693 (467–3959)	< **0.001**
Troponin T, ng/mL, median (IQR; *n* = 404)	< 0.01 (< 0.01–0.02)	< 0.01 (< 0.01–0.01)	0.02 (< 0.01–0.05)	< **0.001**
eGFR, mL/min per 1.73 m^2, median (IQR)	71 (59–82)	74 (64–89)	63 (45–77)	< **0.001**
Serum creatinine ⩾ 2 mg/dL, *N* (%)	27 (6%)	6 (2%)	21 (15%)	< **0.001**
Urinary proteinuria, g/24 h, median (IQR)	2.9 (0.3–7.3)	3.1 (0.2–6.9)	2.6 (0.3–8.4)	0.38
FISH abnormalities, N (%; *n* = 241)				
t (11;14)	131 (54%)	97 (53%)	34 (57%)	0.62
Monosomy/deletion 13	83 (34%)	60 (33%)	23 (38%)	0.46
Any trisomy(ies)	55 (23%)	39 (22%)	16 (27%)	0.41

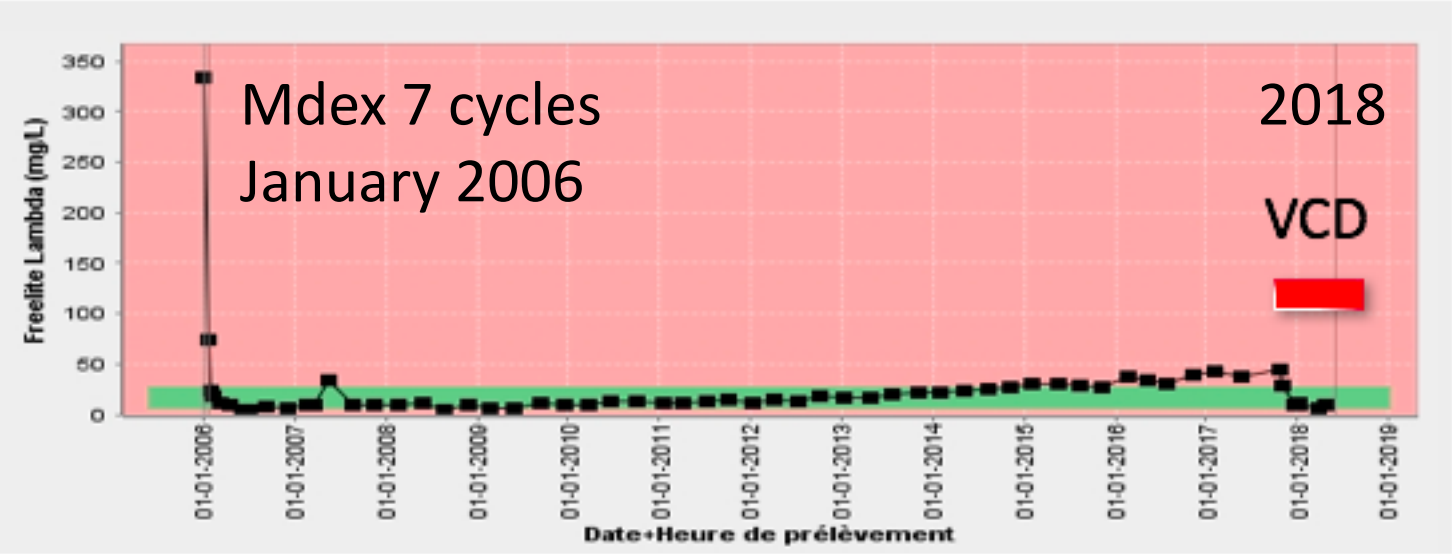
Abbreviations: BMPC = bone marrow plasma cell; dFLC = difference between involved and uninvolved light chains; eGFR = estimated glomerular filtration rate; IQR = interquartile range; NT-proBNP = N-terminal pro b-type natriuretic peptide. Bold indicates statistical significance at $P < 0.05$.

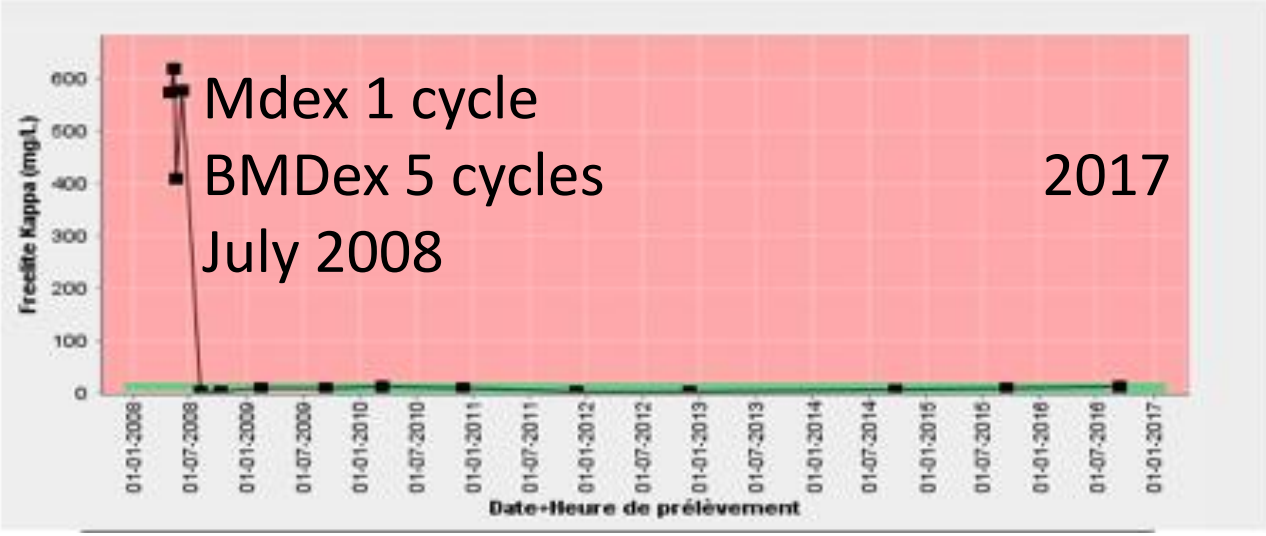
Treatment With Bortezomib-based Therapy, Followed by Autologous Stem Cell Transplantation, Improves Outcomes in Light Chain Amyloidosis: A Retrospective Study

Tania Jain,[1] Heidi E. Kosiorek,[2] Shu T. Kung,[3] Vishal S. Shah,[4] Amylou C. Dueck,[2] Veronica Gonzalez-Calle,[1] Susan Luft,[1] Craig B. Reeder,[1] Roberta Adams,[1] Pierre Noel,[1] Jeremy T. Larsen,[1] Joseph Mikhael,[1] Leif Bergsagel,[1] A. Keith Stewart,[1] Rafael Fonseca[1]

Clinical Lymphoma, Myeloma & Leukemia Month 2018

Is it really worth taking a 5-10% risk of dying within 100 days after ASCT when you can have very long lasting response with conventional treatment

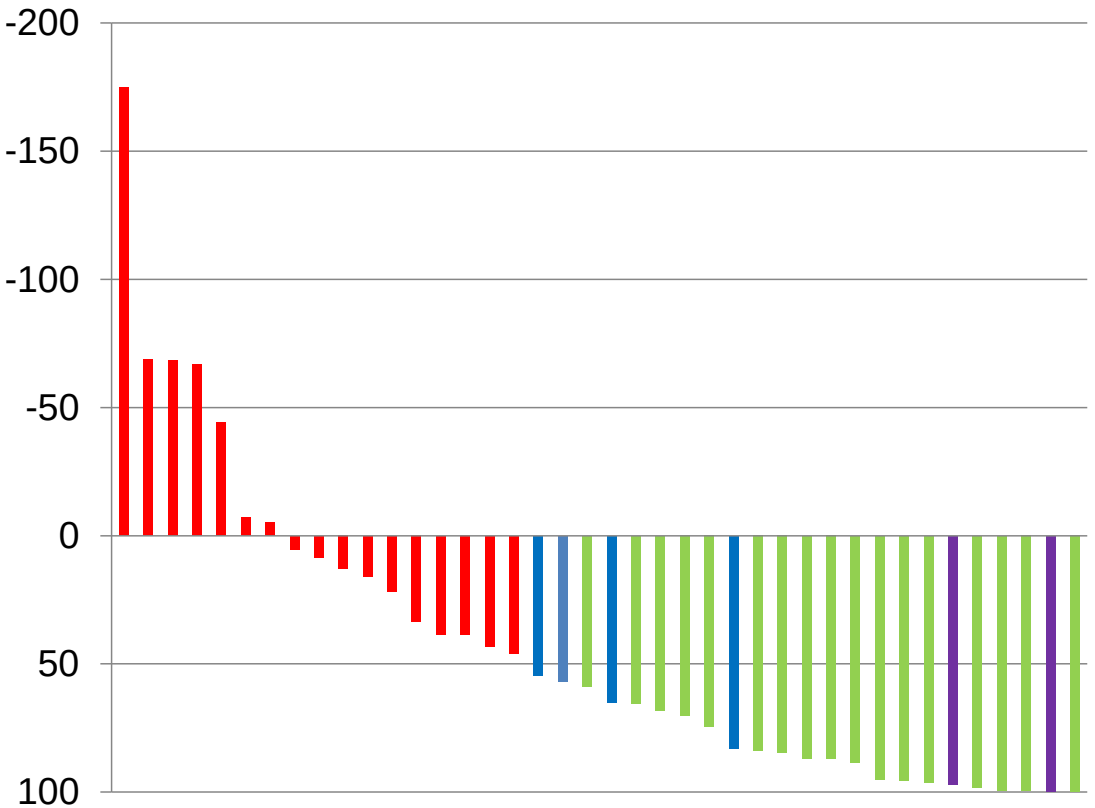




Al amyloidosis therapies, relapse/refractory patients

1965	1995	2000	2003	2006	2012	2016
MP	ASCT	MDEX	Thalidomide CTD	Bortezomib CyborD	Pomalidomide 70%	
30%	65%	65%	65%	80/94% Lenalidomide 60%	Ixazomib Carlfizomib Daratumumab	

Amydara phase II study: 40 patients, median 3 lines of treatment



40 patients

CR	5%
VGPR	43%
PR	10%

58%

Conclusions

- No evidence base medicine to support ASCT in first line in AL amyloidosis
  - Higher TRM
    - 5 to 10 % in expert centers and probably more for centers with less expertise
  - No longer remission duration
  - No better response rate (lower than with bortezomib containing regimen, VCD + Dara ?)

- What is the tiny place of ASCT in this disease
  - Non responding patients with an IgM
  - Patients with a symptomatic multiple myeloma and no severe organ involvement
  - Young patients without severe organ involvement who are refractory to 2 lines of treatment (but daratumumab and venetoclax ??)

ACKNOWLEDGMENTS

- All members of the French network for AL amyloidosis

http//www.cr.amylose-al.fr

N°	Centres	Coordonnateur
1	Hôpital Tenon APHP, Paris	Pr P Ronco Service de Néphrologie et Dialyse
2	Hôpital Saint-Louis, APHP, Paris	Pr JP Fermand Département d'Immunologie Clinique
3	Hôpital Pitié-Salpétrière APHP, Paris	Pr V Leblond Service d'Hématologie Clinique
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6	CHU, Amiens	Dr B Royer Service d'Hématologie Clinique
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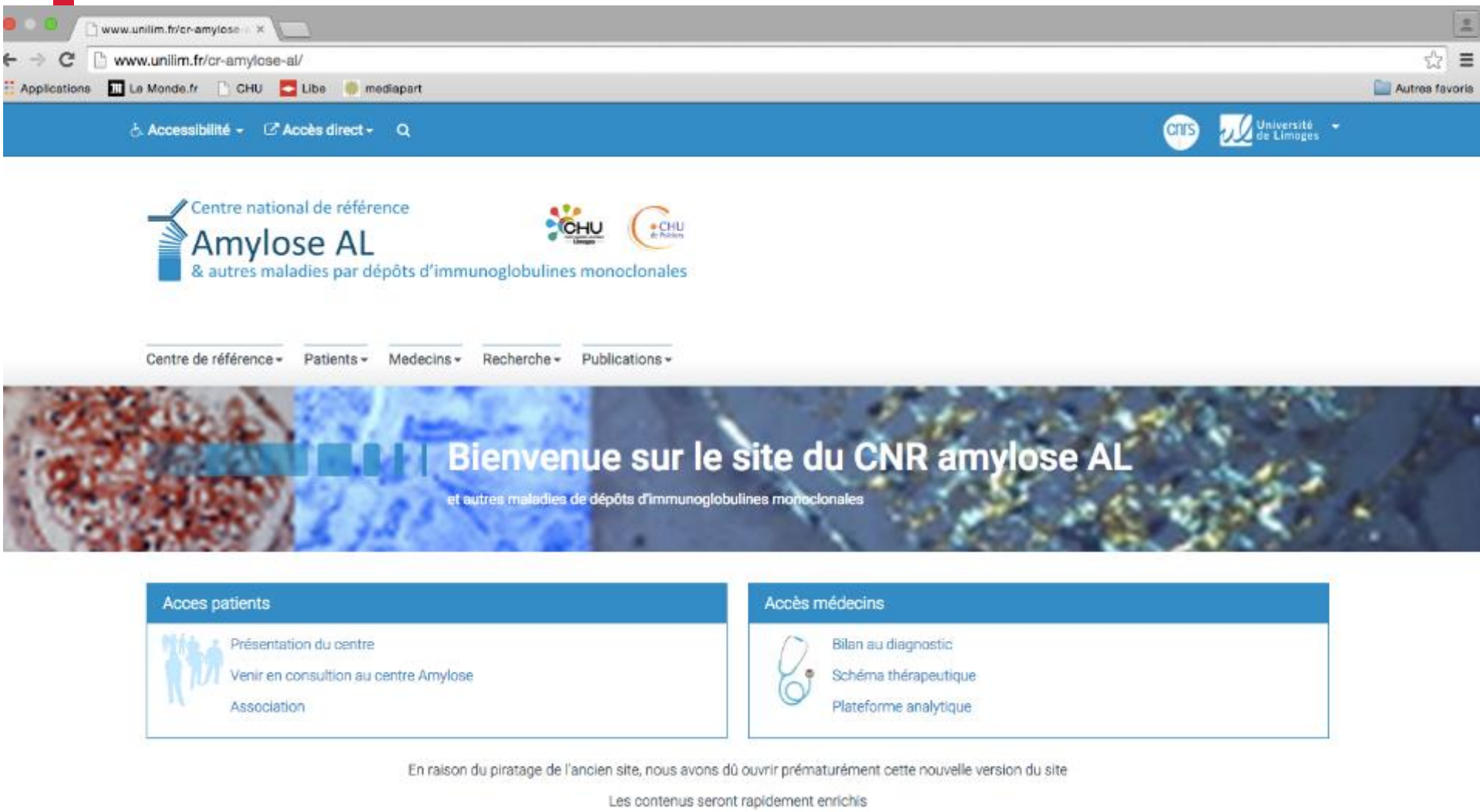
8	CHU, Toulouse	Dr C Recher, Service d'Hématologie Clinique Pr D Chauveau, Service de Néphrologie
9	CHU, Rennes	Pr B Grosbois, Service de Médecine Interne
10	CHU, Strasbourg	Pr B Moulin, Service de Néphrologie
11	Institut Paoli-Calmettes Marseille	Dr AM Stoppa, Service d'Onco-Hématologie II
12	CHU, Angers	Pr N Ifrah, Service des Maladies du Sang,
13	Hôpital Jean Minjoz CHU Besançon -	Pr E Deconinck, Service d'Hématologie Clinique,
14	CHU, Caen	Dr M Macro, Service d'Hématologie Clinique
15	Hôpital Bocage CHU, Dijon	Pr D Caillot, Service d'Hématologie Clinique
16	Réseau Rhône-Alpes Hôpital Edouard Herriot, Lyon	Pr J Ninet, Service de Médecine Interne,
17	CHU Lapeyronie, Montpellier	Pr JF Rossi Service d'Hématologie Clinique et Biothérapies
18	CHU Nancy	Dr C Hulin, Service d'Hématologie
19	Hôpital de l'Archet 1, Nice	Pr JG Fuzibet, Service de Médecine Interne Cancérologie, Hôpital de l'Archet 1, Nice
20	Hôpital Robert Debré CHU Reims	Dr B Kolb, Service d'Hématologie Clinique
21	Centre Henri Becquerel Rouen	Dr F Jardin, Service d'Hématologie Clinique
22	Hôpital Bretonneau CHU Tours	Dr L Benboubker Service d'Hématologie et Thérapie Cellulaire



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