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CARFI study

Carfilzomib and dexamethasone maintenance prolong time to progression following salvage ASCT in multiple myeloma: A randomized phase 2 trial by the Nordic Myeloma Study Group

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CARFI

Disclosures

Henrik Gregersen: None

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Gregersen H, et al. Oral presented at: EHA Annual Meeting; June 13-16, 2019; Amsterdam, Netherlands.

CARFI - Introduction

High-dose melphalan with autologous stem cell transplantation (ASCT) is a well established treatment at diagnosis in younger myeloma patients

Salvage ASCT is an option for some patients (PFS 1 > 18 months)

The evidence for salvage ASCT is sparse

Gregersen H, et al. Oral presented at: EHA Annual Meeting; June 13-16, 2019; Amsterdam, Netherlands.

CARFI - Introduction

The optimal induction treatment before salvage ASCT is unknown – use of the same induction treatment often results in half the length of response

Carfilzomib is a next generation proteasome inhibitor with an important role in treatment of multiple myeloma

Gregersen H, et al. Oral presented at: EHA Annual Meeting; June 13-16, 2019; Amsterdam, Netherlands.

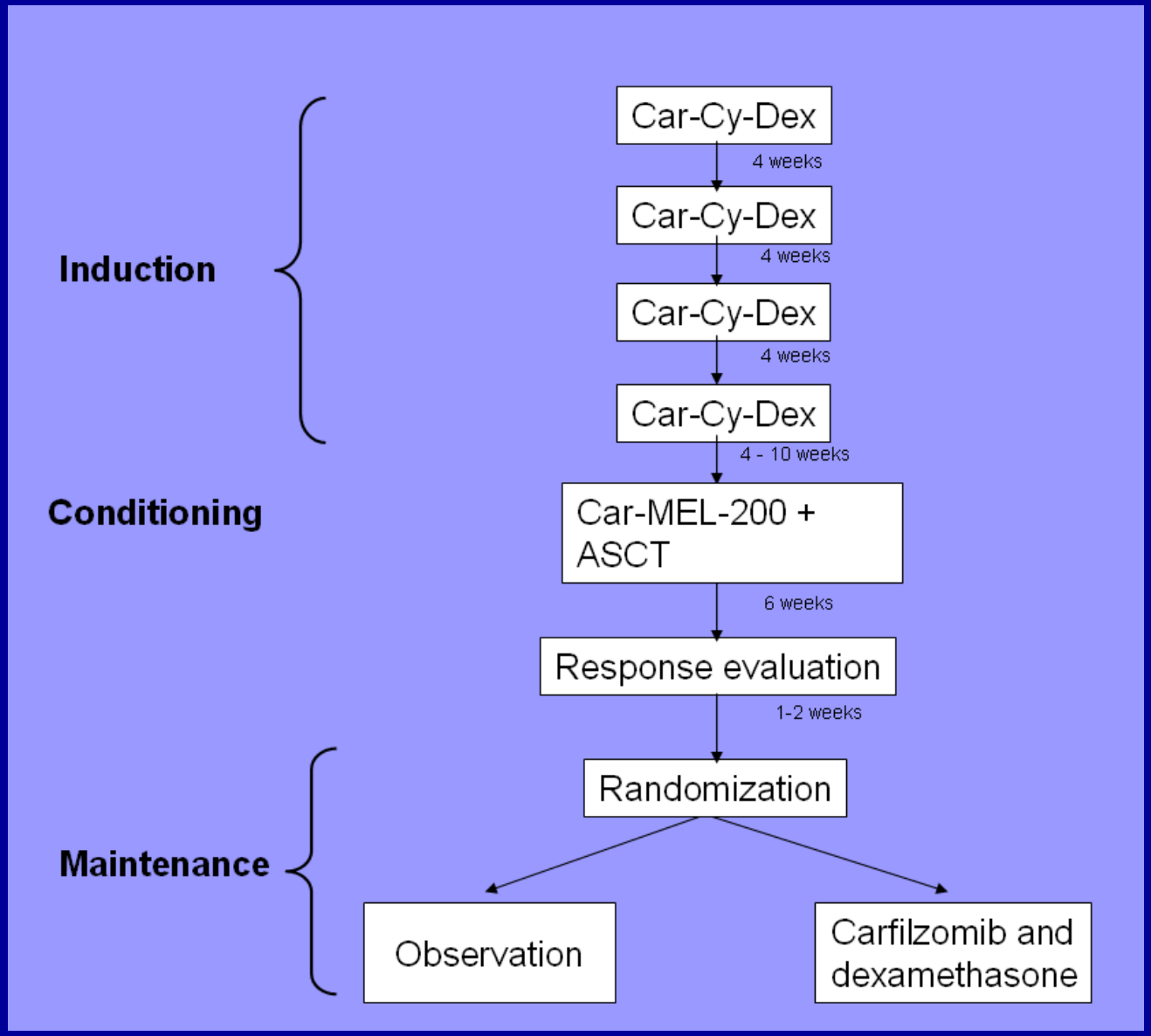
CARFI - Introduction

Lenalidomide maintenance after ASCT at diagnosis is considered standard of care

There are limited data on the role of maintenance therapy after salvage ASCT

<u>Small phase 1-2 study</u>: 27 patients received carfilzomib maintenance 36 mg/sqm either 3 or 4 times in 4-week cycles.
12-month progression-free survival was 66.7%
Costa et al. Biol Blood Marrow Transplant 2018

CARFI - Study design



Carfilzomib 20 → 36 mg/sqm

Carfilzomib 27 mg/sqm

Carfilzomib 27 → 56 mg/sqm

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CARFI – two primary endpoints

Comparison of time to progression after high-dose melphalan with stem cell support at diagnosis and time to progression after salvage ASCT combined with carfilzomib-cyclophosphamide-dexamethasone (CAR-CY-DEX)

Comparison of time to progression between carfilzomib-dexamethasone maintenance and observation in patients treated with a salvage ASCT

Gregersen H, et al. Oral presented at: EHA Annual Meeting; June 13-16, 2019; Amsterdam, Netherlands.

CARFI: Key inclusion criteria

First treatment demanding relapse after ASCT done at diagnosis

More than 2.0 x 10^6 CD34+ stem cells / kg body weight in the freezer for stem cell support

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CARFI: Key exclusion criteria

Treatment demanding relapse less than one year after ASCT

Myeloma treatment after the first ASCT, except radiotherapy, bisphosphonates, denosumab and corticosteroids less than 6 days for symptom control

No former carfilzomib treatment

Significant neuropathy/performance status (WHO) ≥ 3

Comorbidity that would preclude treatment with carfilzomib or ASCT

Gregersen H, et al. Oral presented at: EHA Annual Meeting; June 13-16, 2019; Amsterdam, Netherlands.

CARFI - status

200 patients included from January 2015 to April 2018 at 24 sites in Denmark, Norway, Sweden, Finland and Lithuania

86 randomised to observation
82 randomised to maintenance
32 not randomised for various reasons

Study will stop 1 September ≈ 9 months after last randomisation

Gregersen H, et al. Oral presented at: EHA Annual Meeting; June 13-16, 2019; Amsterdam, Netherlands.

CARFI - Baseline characteristics

Number	200
Age (median age, IQR)	62 (56 – 66)
Time from MM diagnosis (months)	41.3 (30.0 – 58.4)
Previous treatment	
VAD	1 (0.5%)
CY-DEX	4 (2%)
CY—VEL-DEX (=VCD)	145 (72.5%)
CY – THAL - DEX	12 (6%)
VEL-DEX	22 (11%)
Other	16 (8%)
Bone disease	166 (83%)
Performance status I - II	183 (91.5%)
High-risk cytogenetics	39 (19.5%)
ISS	18 (9%)

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CARFI – time to progression

	1. ASCT (% 18 months relapse free)	Salvage ASCT (%18 months relapse free)
Progression	93.5 (90.1-97.0)	72.7 (65.5-80.6)

Median time to progression (months)	33.2 (30.8-37.7)	28.1 (25.1-31.5)

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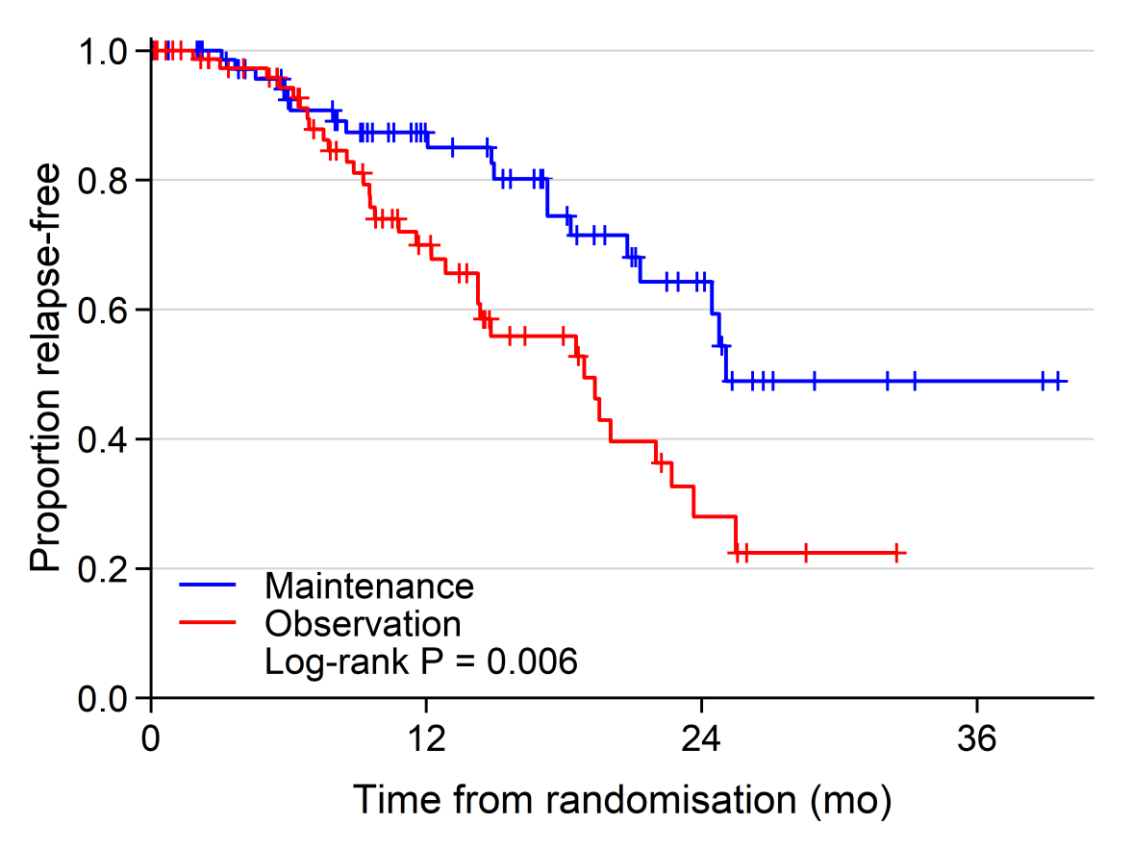
CARFI – maintenance/observation



Median time to progression:

Observation: **18.9 months (14.3 – 23.3)**

Maintenance: **25.1 months (24.4 – NR)**

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CARFI – discontinuation

Induction and ASCT (200 patients)	
Cardiac adverse events	3 (1.5%)
Fatal infection	4 (2%)
Other adverse events	3 (1.5%)
Frail condition	3 (1.5%)
Minor response	2 (1%)
Progression	8 (4%)
Withdrawal of consent	7 (3.5%)
Non-compliance	1 (0.5%)
Broken bag of stem cells	1 (0.5%)
Total	32 (16%)

Observation (86 patients)	
Progression	30 (34.9%)
Withdrawal of consent	1 (1.2%)
Total	31 (36%)

Maintenance (82 patients)	
Progression	20 (24.4%)
Withdrawal of consent	3 (3.7%)
Adverse events	5 (6.1%)
Total	28 (34.1%)

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CARFI – serious adverse events

	Maintenance (82)	Observation (86)
Cardiac and pulmonary	**3**	**1**
Syncope	1	
Atrial fibrillation	1	
Pulmonary embolism	1	
Dyspnea		1
Infection	**35**	**21**
Viral	10	2
Septicemia	2	0
Pneumonia	10	6
Airway, other	3	5
Fever	5	8
Misc infections	5	0
Misc SAEs	**9**	**4**
Total	**47**	**26**

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CARFI – conclusion

Maintenance therapy with carfilzomib and dexamethasone maintenance prolongs median time to progression with approximately 6 months following salvage ASCT in multiple myeloma.

An increased number of SAEs was observed in the maintenance arm, mainly infections

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