

A Phase II Trial of Myeloma Induction Therapy With Cyclophosphamide, Bortezomib and Dexamethasone (Cybor-D): Improved Response Over Historical Lenalidomide-Dexamethasone Controls

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Disclosure Statement

Employment: no

Consultancy: yes, Fonseca, Stewart, Reece

Ownership: no

Ownership Interest: no

Research funding: yes, Reeder, Stewart for this trial

Honoraria: no

Financial relationship: no

Off label use: yes, Bortezomib in newly diagnosed MM

Background

- Cyclophosphamide (Cy), Bortezomib (BZ) and Dexamethasone (Dex) all have single agent activity in Multiple Myeloma (MM)
- Stewart et al. previously reported an 85% response rate with 54% CR in relapsed MM using a combination of Cy, BZ and prednisone
- Rationale: Cy, BZ and Dex should have significant activity in newly diagnosed patients with MM

Study Goal

- Response rates: CR, nCR, VGPR
- Overall response
- Progression free and overall survival
- Toxicity of the CyBor-D regimen

Schema

Newly Diagnosed Myeloma



Cyclophosphamide 300 mg/m² p.o. weekly, days 1, 8, 15, 22
Bortezomib 1.3mg/m² i.v. days 1, 4, 8, 11
Dexamethasone 40mg p.o. days 1 – 4, 9 – 12, 17 – 20
(Q28 day cycles)



4 cycles (16 weeks)



Response Assessment



***Stem cell Collection**



Off Study To Transplant



OR
8 cycles

Continue Meds for further

Methods

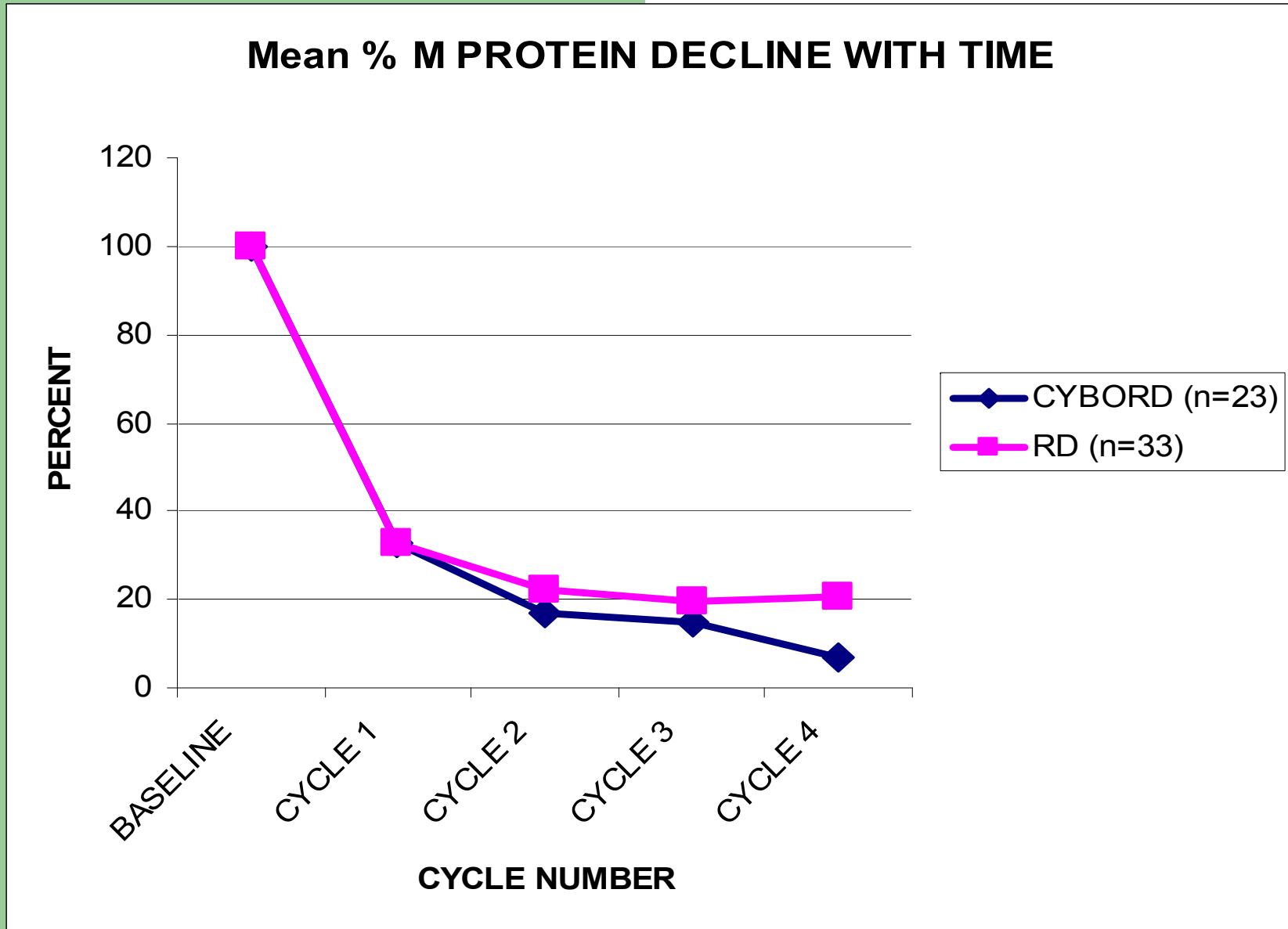
- 33 patients enrolled to date
- 23 evaluable for response and toxicity after at least one cycle of CyBor-D
- 14/30 have completed 4 cycles
- Response defined according to IMWG criteria though bone marrows are not yet available for all patients to confirm CR
- Responses are compared to a control group who received what many consider a standard induction regimen of Lenalidomide and Dexamethasone (L-Dex) (Rajkumar, Blood, 2005;106:4050-3)

Updated Response - % decline in M-protein

Table 4

CyBor-D	66	83	85	93
L-Dex	67	78	81	80

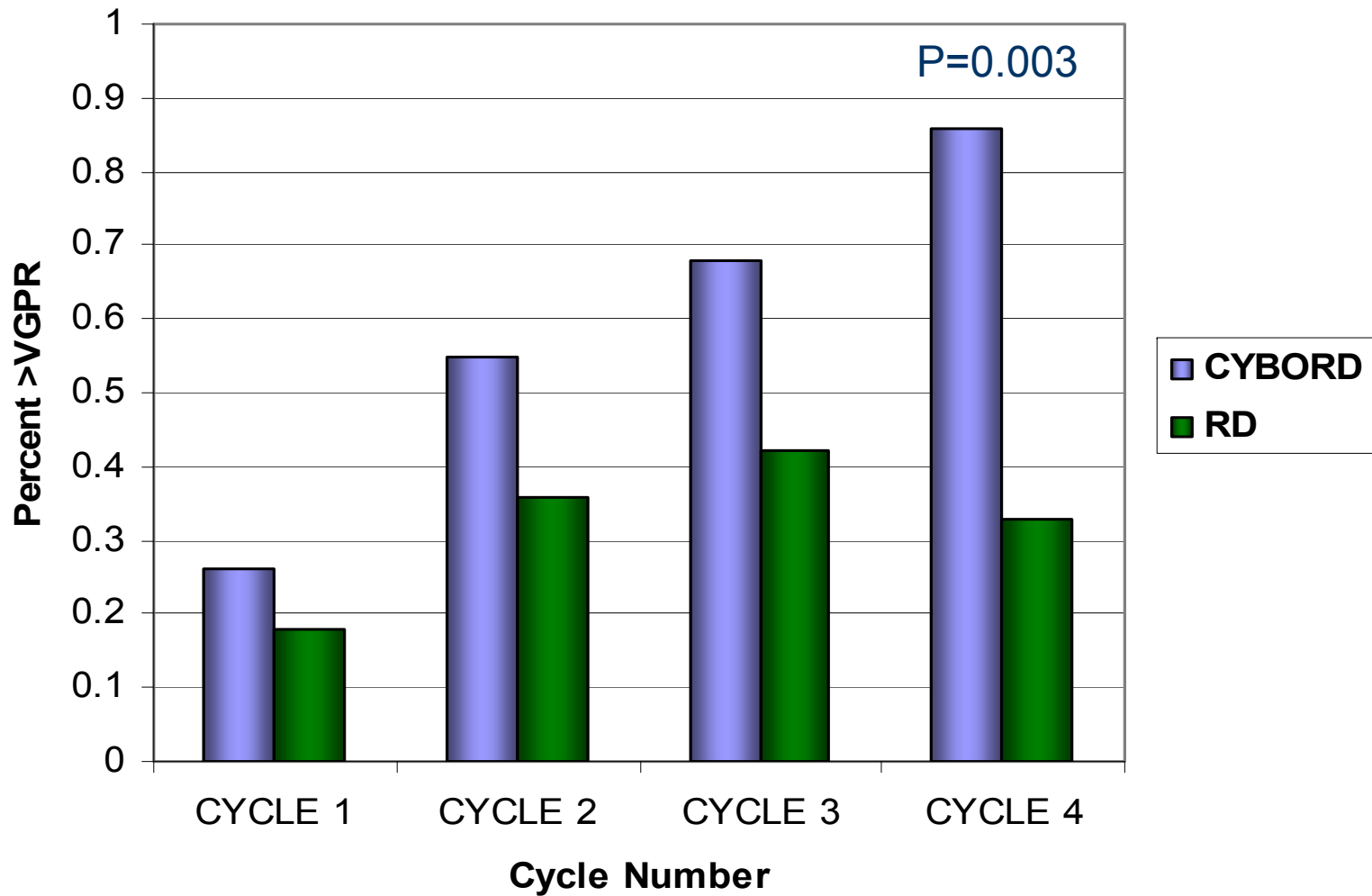
CYBOR-D – SPEED AND DEPTH OF RESPONSE IS SUPERIOR TO Rev-Dex



Updated Response - % in \geq VGPR after each cycle

	Cycle 1	Cycle 2	Cycle 3	Cycle 4
CyBor-D	26	55	68	86
L-Dex	18	36	42	33

VGPR or Better by Cycle



Response after Cycle 4

- **CR** **1/14 (7%)** **5/30 (17%)**
- **NCR** **8/14 (57%)** **1/30 (3%)**
- **VGPR** **3/14 (21%)** **4/30 (13%)**
- **PR** **2/14 (14%)** **16/30 (53%)**
- **MR** **0/14 (0%)** **1/30 (3%)**
- **SD/NR** **0/14 (0%)** **3/30 (10%)**

At least nCR in 64% of patients

Results – Toxicity

- ≥ Gr 3 hematologic 24%, neutropenia 20%
- ≥ Gr 3 hyperglycemia 17%
- ≥ Gr 3 sensory neuropathy 5%
- Overall incidence of neuropathy 69%
- ≥ Gr 3 Infection 5%

Conclusions

- CyBor-D induction therapy is highly active in newly diagnosed MM
 - *64% in CR or nCR and 86% in VGPR or better after 4 cycles*
- CyBor-D produces more profound responses than the best standard therapy, Lenalidomide and dexamethasone
- CyBor-D has manageable toxicities