Improved Overall Survival (OS) with Oral Selinexor Plus Low Dose Dexamethasone (Sd) in Patients with Triple Class Refractory-Multiple Myeloma (TCR-MM) compared to FLATIRON – Real World Evidence

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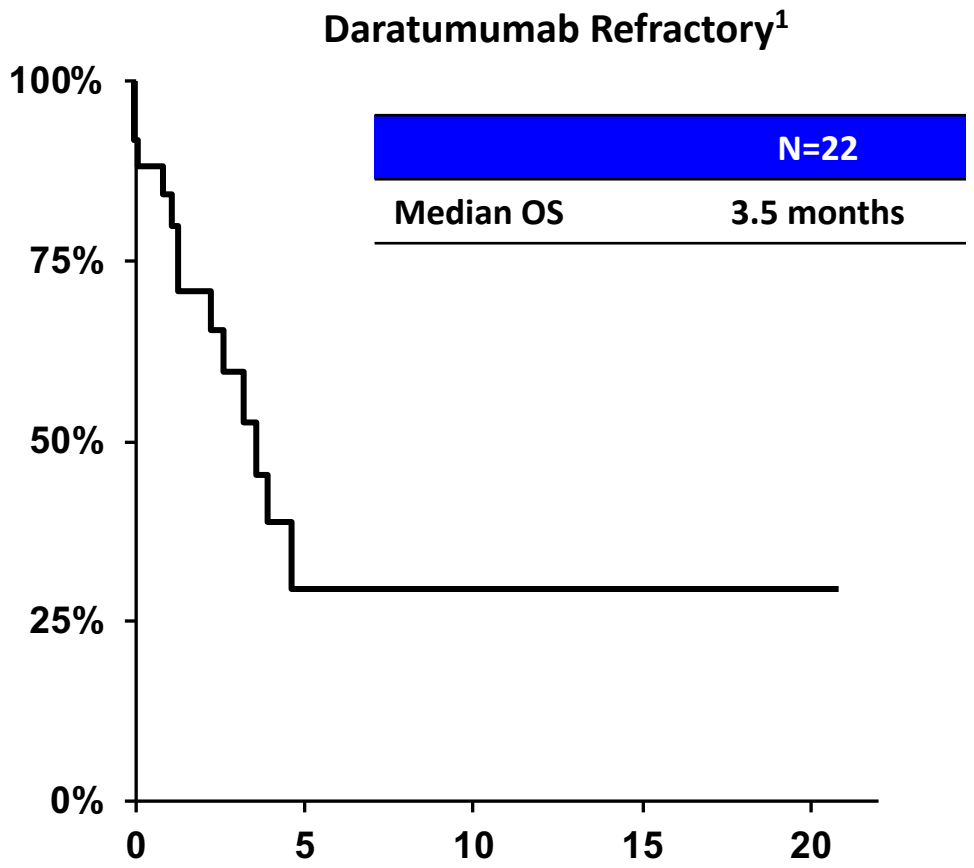
Background – TCR-MM

Triple-Class Refractory Multiple Myeloma (TCR-MM):

- A growing number of patients are exposed to the proteasome inhibitors (PIs) bortezomib and carfilzomib, the immunomodulatory (IMiDs) agents lenalidomide and pomalidomide, and the anti-CD38 monoclonal antibody daratumumab
- TCR-MM is defined as myeloma that is refractory to an IMiD (lenalidomide and/or pomalidomide), a PI (bortezomib and/or carfilzomib), and the anti-CD38 mAb daratumumab
- TCR-MM represents an unmet medical need with median overall survival of 3.5 months (*Pick[1] M et al., Eur J Haematol. 2018*)



Background – Selinexor

Selinexor is an oral selective **XPO1 inhibitor**:

- Exportin 1 (XPO1) transports >200 proteins from the nucleus to cytoplasm including tumor suppressor proteins (TSPs)
- Selinexor reactivates multiple TSPs by preventing nuclear export
- Selinexor also reactivates glucocorticoid receptor signaling with the presence of dexamethasone

STORM Study:

- A Phase 2b study in which patients with MM previously treated with bortezomib, carfilzomib, lenalidomide, pomalidomide, daratumumab, an alkylator, a glucocorticoid, and had documented disease refractoriness to ≥1PI, ≥1 IMiD, and daratumumab were enrolled
- Selinexor (80 mg) in combination with low-dose dexamethasone (20 mg) was administered twice-weekly (Days 1 and 3 – 28 day cycle)
- Selinexor in combination with dexamethasone (Sd) showed a **26.2%** overall response rate (ORR) in 122 patients with penta-exposed TCR-MM (Chari A et al., ASH 2018)
  - The ORR in patients with penta-refractory disease (2 PIs, 2 IMiDs, and dara refractory) was **25.3%** in 83 patients

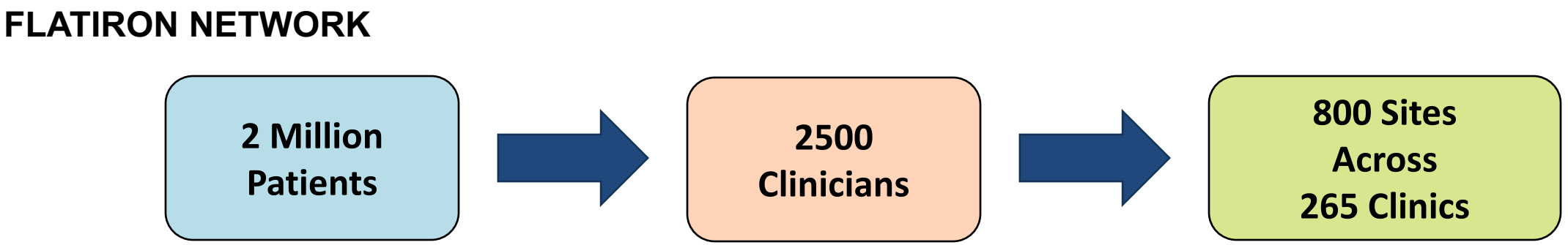
Flatiron Health Analytic Database (FHAD)

Flatiron Health Analytic Database (FHAD):

- The Flatiron Health Analytic Database (FHAD) is an oncology platform that aggregates electronic health records (EHRs) data from patients within the Flatiron network

- Flatiron provides real-world clinical data collected from EHRs used by cancer care providers, including community and academic cancer centers, across the United States

- Flatiron uses a technology-enabled abstraction and multi-pronged quality assurance approaches to generate research-ready datasets (*Berger 2016, Friends of Cancer Research 2016*)



Methods

Objective: Evaluate the overall survival of patients in the STORM study treated with Sd as compared to patients from an observational cohort (FHAD) with TCR-MM not treated with Sd

- Patient data was drawn from the STORM study (N=122) and patients were identified from FHAD (N=69) who mimicked patients on the STORM study
- All patients from both groups had penta-exposed TCR-MM and had ≥1 therapy after reaching penta-exposed TCR status

FHAD Patient Selection Requirements:

- ≥ 2 documented clinical visits since 01 January 2011 and pathology consistent with multiple myeloma
- Documented treatment with bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab (penta-exposed)
- Documented as triple-class refractory (refractory to at least 1 PI, 1 IMiD, and daratumumab)

FHAD & STORM Index Date Definition:

- Defined as the start date of treatment after the patient's myeloma reached penta-exposed TCR status and then received treatment with Sd (STORM patients) or ≥1 therapy (FHAD patients)

- STORM **N=64**
- FHAD **N=36**

STORM *vs.* FHAD Patient Comparison

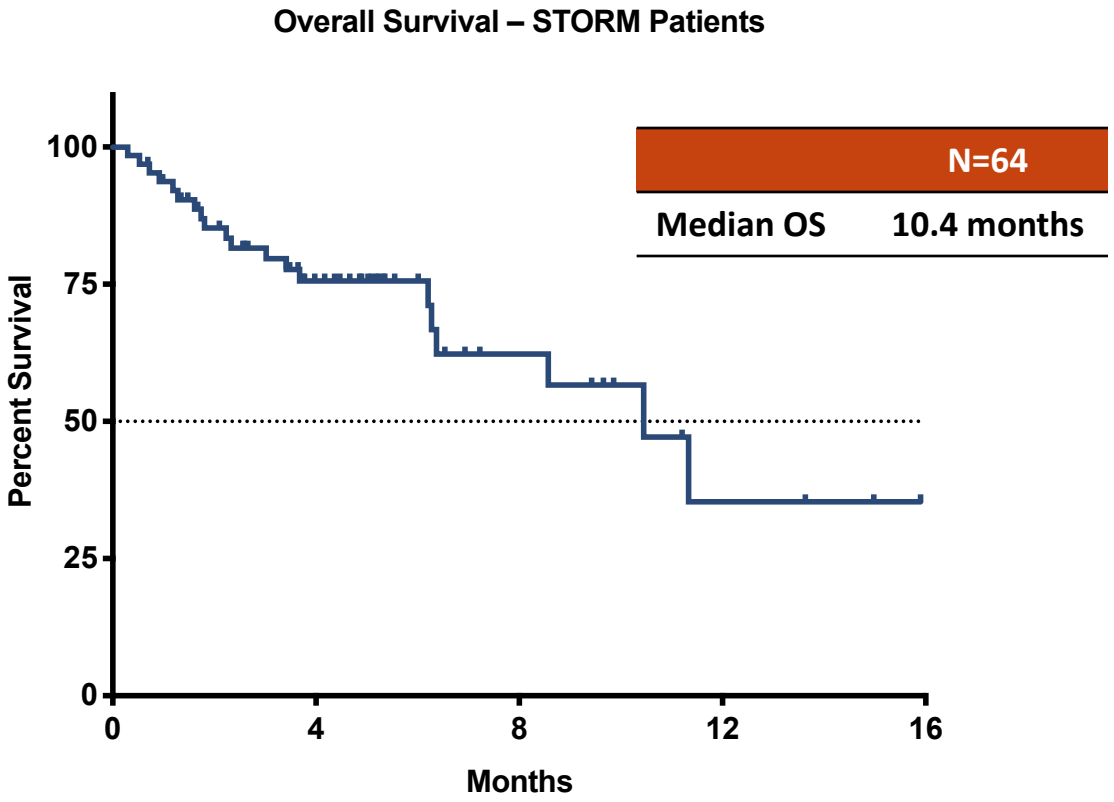
Characteristic	STORM (N=64)	FHAD (N=36)
Age (years), median	65	64
<65	31 (48%)	18 (50%)
≥65	33 (52%)	18 (50%)
Male : Female	33 (52%) : 31 (48%)	19 (53%) : 17 (47%)
Race		
White	34 (53%)	22 (61%)
Non-White	30 (47%)	14 (39%)
Black or African American	15 (23%)	5 (14%)
Carfilzomib, Pomalidomide, and Daratumumab Refractory Prior to Index Date	60 (94%)	20 (56%)
Number of Prior Regimens, median (range)	6 (3, 18)	5 (2, 7)
Exposed to Anthracyclines Prior to Index Date	19 (30%)	4 (11%)
Exposed to Alkylating Agent Prior to Index Date	64 (100%)	21 (58%)
Stem Cell Transplant Prior to Index Date	53 (83%)	22 (61%)
Baseline Hemoglobin (g/dL), median (range)	10.4 (8.1, 14.3)	9.5 (6.0, 14.1)
Baseline Platelets (x10^9/L), median (range)	213 (53, 390)	124 (12, 459)

STORM *vs.* FHAD Patient Comparison

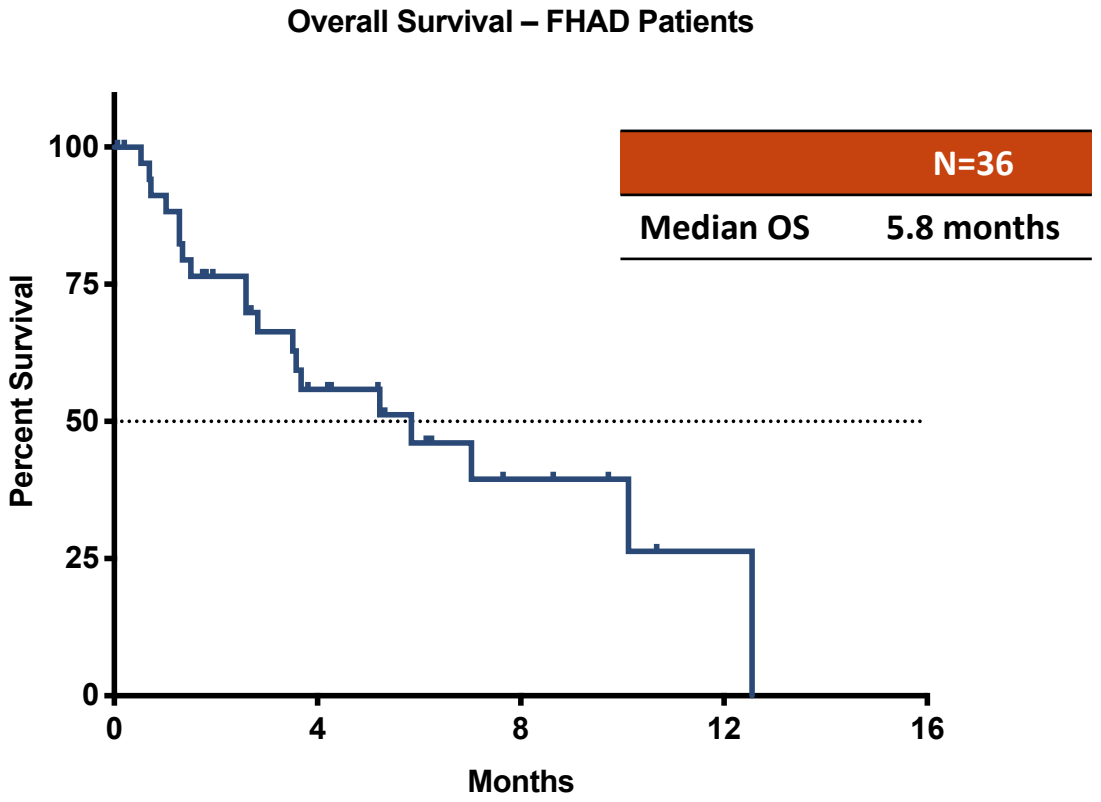
The patients in STORM and FHAD populations were well balanced, however patients in STORM had more refractory disease:

- 94% (STORM) *vs.* 56% (FHAD) of patients with disease refractory to Carfil/Pom/Dara
- 100% (STORM) *vs.* 58% (FHAD) had prior alkylating therapy

STORM *vs.* FHAD Overall Survival



Months	0	4	8	12	14	16
Pts at Risk	64	33	11	3	2	0



Months	0	4	8	10	12	14
Pts at Risk	36	15	5	3	1	0

Cox proportional hazards regression model was performed to assess the survival impact of treatment with Sd. The median OS (N=64) was **10.4** months for patients receiving Sd in STORM and **5.8** months (N=36) for patients not receiving Sd in the FHAD cohort with a Hazard Ratio=0.51, (p=0.036)

STORM *vs.* FHAD Overall Survival – Sensitivity Analyses

Analysis* #	FHAD Patients #	FHAD Median OS 95% CI (months)		STORM Patients #	STORM Median OS 95% CI (months)		Hazard Ratio 95% CI		*p-value*
1	**35**	5.9	(2.60, 12.6)	**64**	10.4	(6.28, NE)	0.525	(0.28, 0.99)	*0.0476*
2	**28**	5.9	(3.52, 12.6)	**62**	10.4	(6.28, NE)	0.539	(0.28, 1.06)	*0.0719*
3	**34**	5.2	(2.60, 10.1)	**63**	10.4	(6.28, NE)	0.449	(0.24, 0.84)	*0.0129*
4	**30**	5.9	(2.60, 12.6)	**64**	10.4	(6.28, NE)	0.551	(0.28, 1.08)	*0.0814*
5	**25**	10.1	(2.60, 12.6)	**64**	10.4	(6.28, NE)	0.621	(0.30, 1.30)	*0.2051*
6	**21**	5.9	(1.51, 12.6)	**64**	10.4	(6.28, NE)	0.521	(0.25, 1.09)	*0.0827*
7	**22**	5.9	(2.60, 12.6)	**53**	10.4	(6.37, NE)	0.442	(0.21, 0.95)	*0.0357*
8	**34**	5.9	(2.83, 12.6)	**51**	10.4	(6.28, NE)	0.555	(0.28, 1.10)	*0.0921*
9	**36**	5.9	(2.83, 12.6)	**40**	10.4	(3.68, NE)	0.620	(0.32, 1.21)	*0.1627*

*Analysis type: **1)** exclude patients with concomitant plasma cell leukemia; **2)** adequate hepatic function; **3)** adequate renal function; **4)** platelet count ≥50,000 mm^3; **5)** hemoglobin >8 g/dL; **6)** prior alkylating agent treatment; **7)** prior stem cell transplant; **8)** exclude 17p deletion patients; **9)** ≤7 prior treatment regimens

Overall Survival Sensitivity Analyses:

- Different inclusion / exclusion criteria were selected to adjust the patient population and to assess the impact on median OS, HR, and p-values
- Comparisons were done by applying STORM inclusion / exclusion criteria to both populations. Advanced analytic methods for covariate adjustment were not done due to small sample size.

Conclusions

- To best provide perspective and contextualize the overall survival seen in STORM we compared outcomes in STORM to real-world evidence using the validated FLATIRON database
- To remove biases the patient population was matched and the index date was defined as when patients became first TCR and received subsequent therapy after having TCR disease
- The median OS of patients receiving Sd as their first therapy after their MM becomes TCR is 10.4 months and almost twice as long as those receiving SOC therapy (5.8 months)
- Sd when patients first become TCR may be associated with an OS benefit