Selinexor
SINEs in Multiple Myeloma

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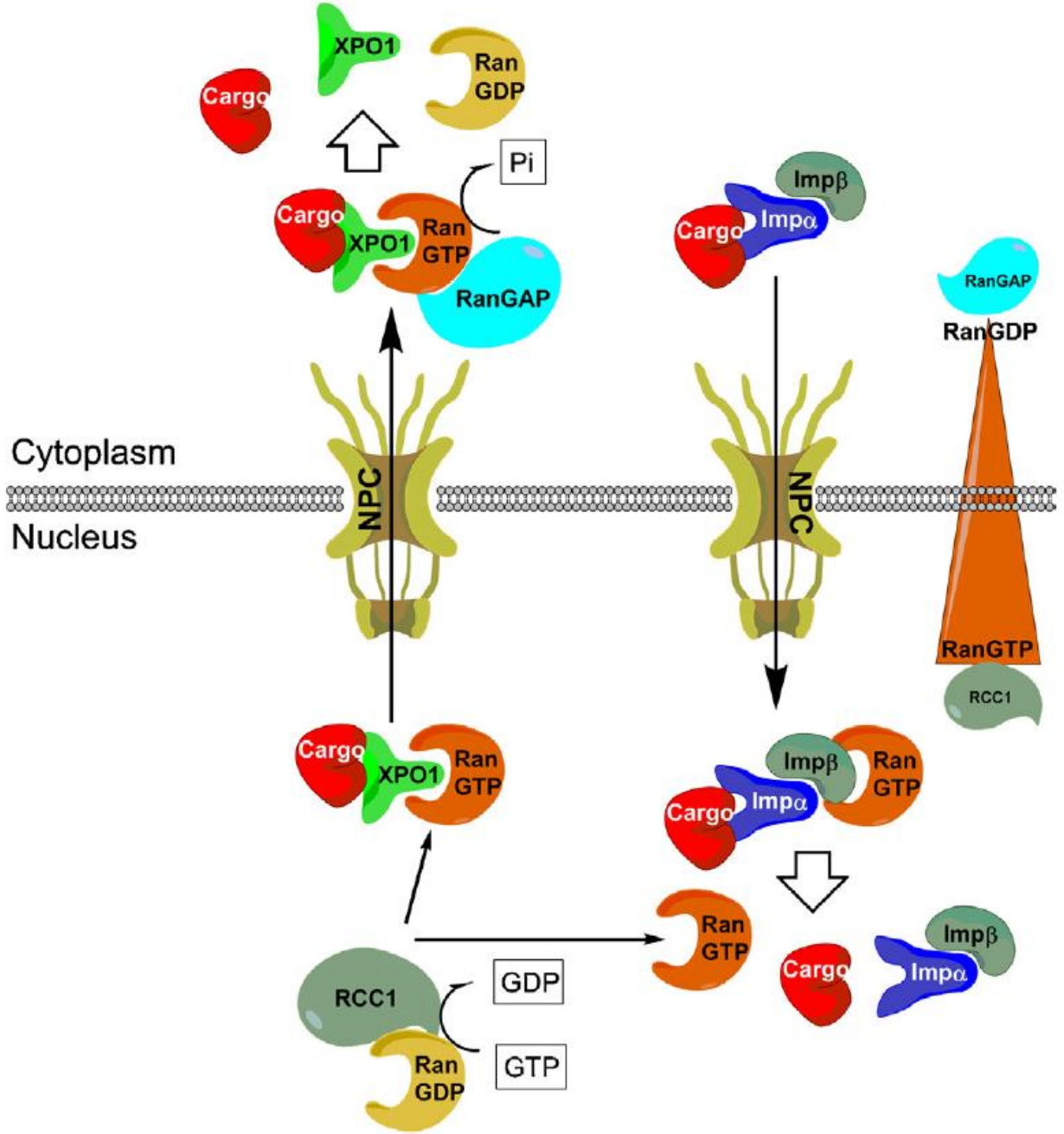
Bologna 2018

UNIVERSITY OF
CALGARY

Model of the mammalian nuclear pore complex

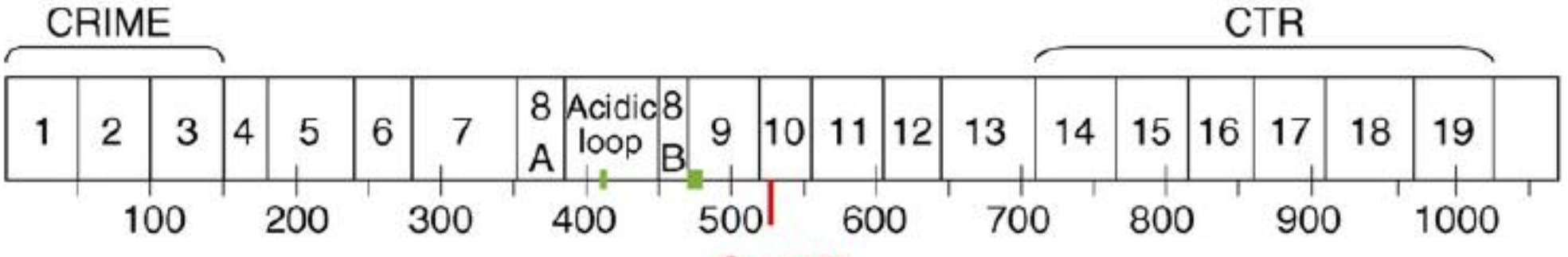


CRM1 (Chromosomal Maintenance 1, Exportin 1 or XPO1) is the major mammalian export protein.

XPO1 facilitates the transport of large macromolecules including RNA and protein across the nuclear membrane to the cytoplasm.

Stade et al, Cell 1997
Adachi et al, The Journal of Cell Biol 1989
Hutten et al Trends in Cell Biology 2007

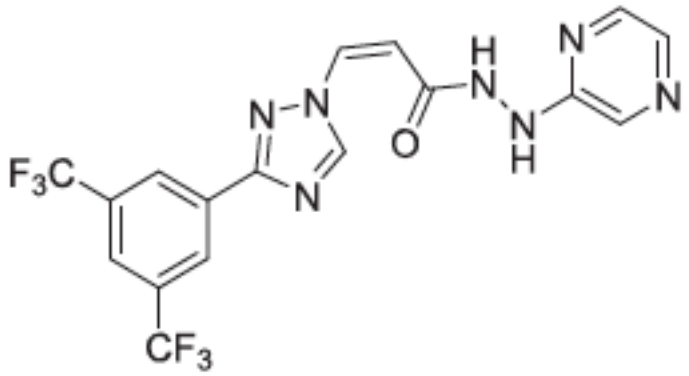
Small-molecule selective inhibitors of nuclear export (SINEs)



Cys528

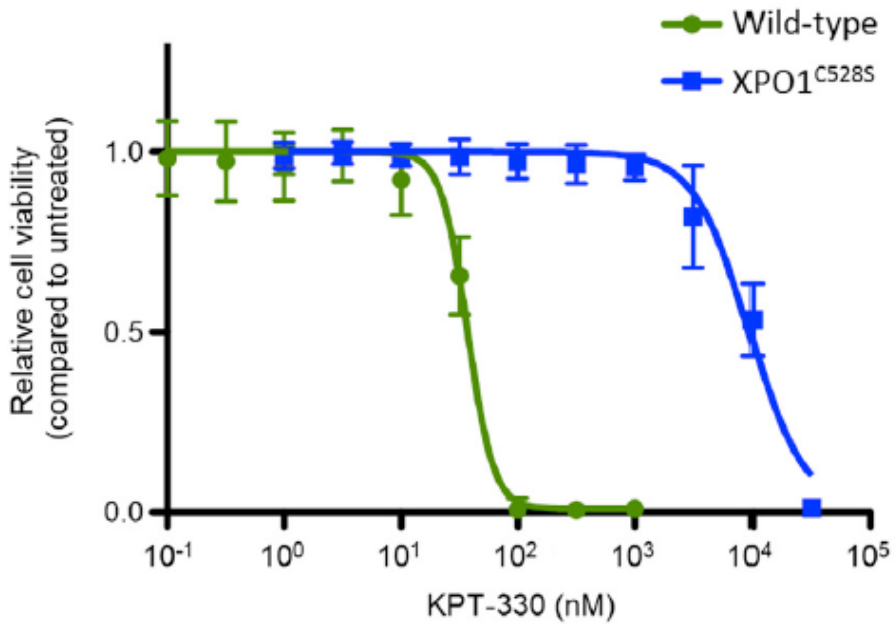
LMB

KPT-330



Chemical Formula: $C_{17}H_{11}F_6N_7O$

Molecular Weight: 443.31

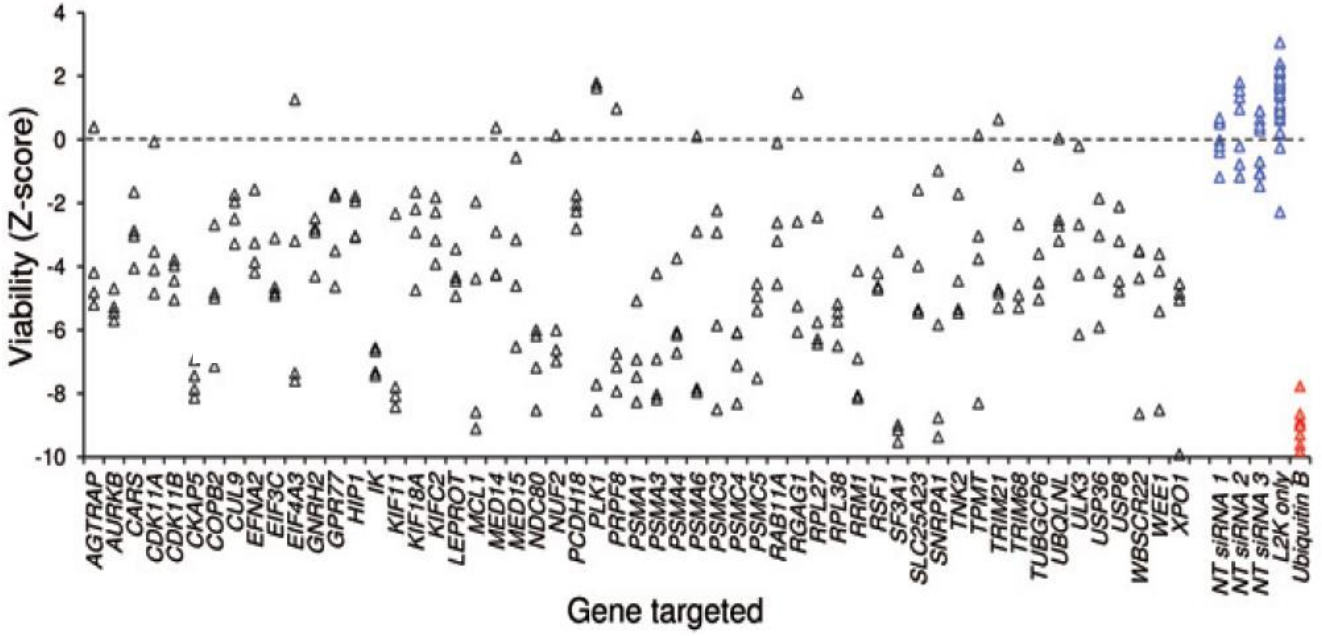


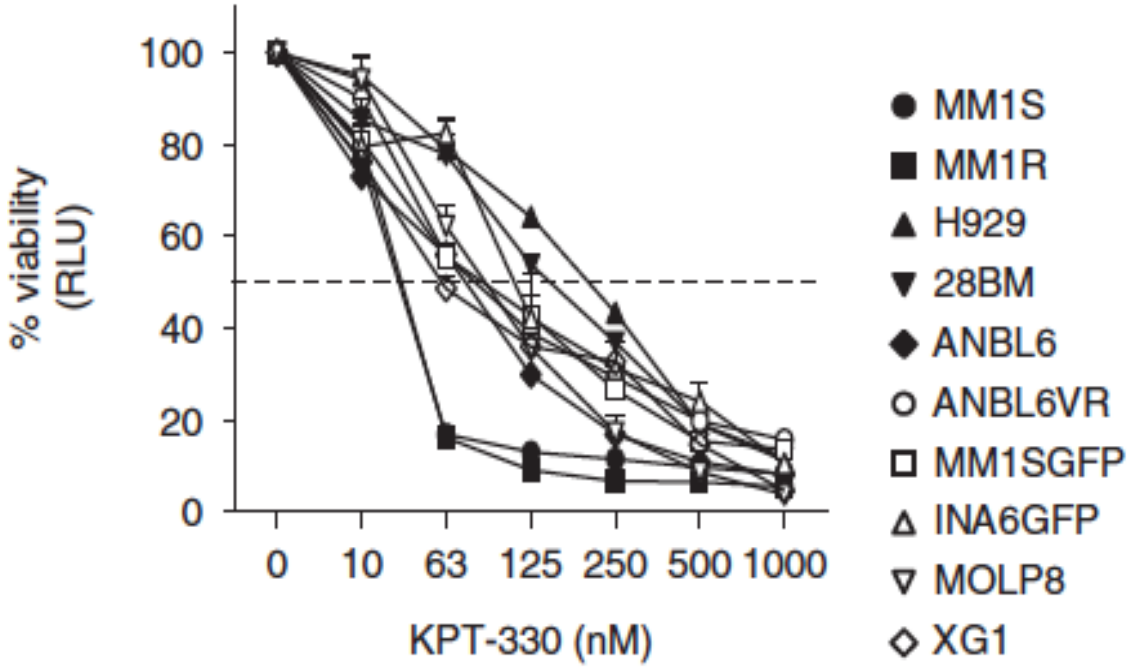
Kalid et al, J Comput Aided Mol Des 2012

Neggers et al, Chemistry & Biology 2015

XPO1as therapeutic target in Myeloma

Synergy with Proteasome inhibitors





Tiedemann et al Cancer Research 2011
Schmidt et al, Leukemia 2013
Tai et al, Leukemia 2014

XPO1as therapeutic target in Myeloma

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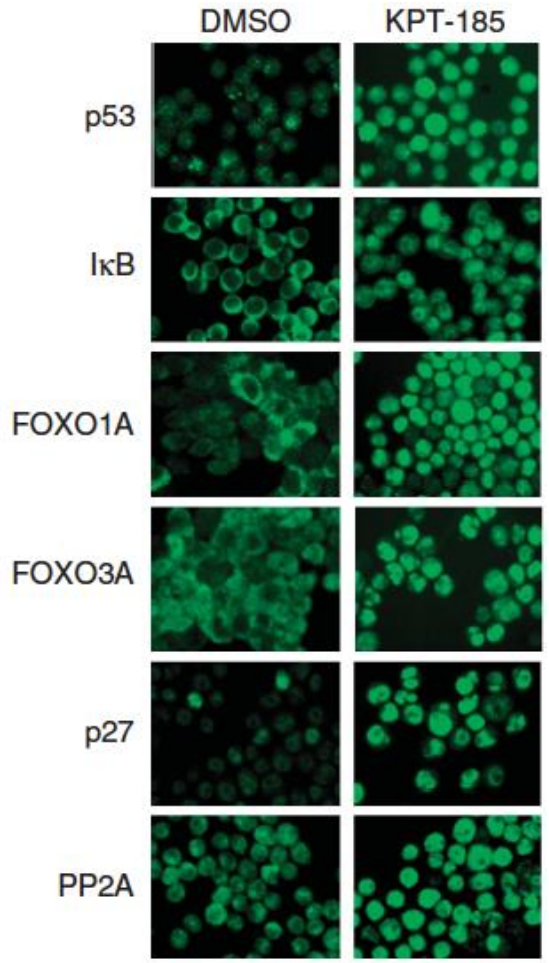
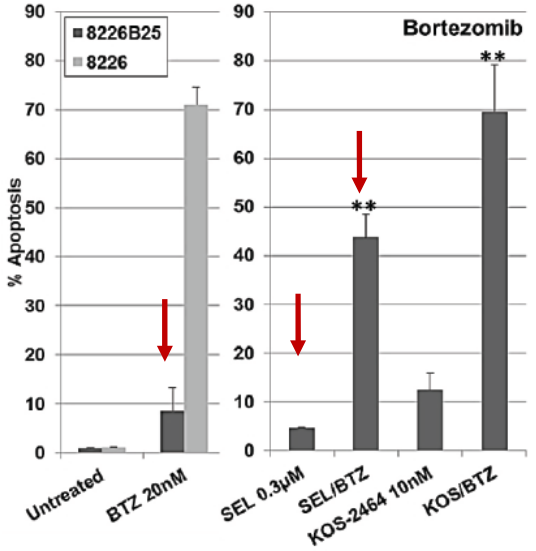
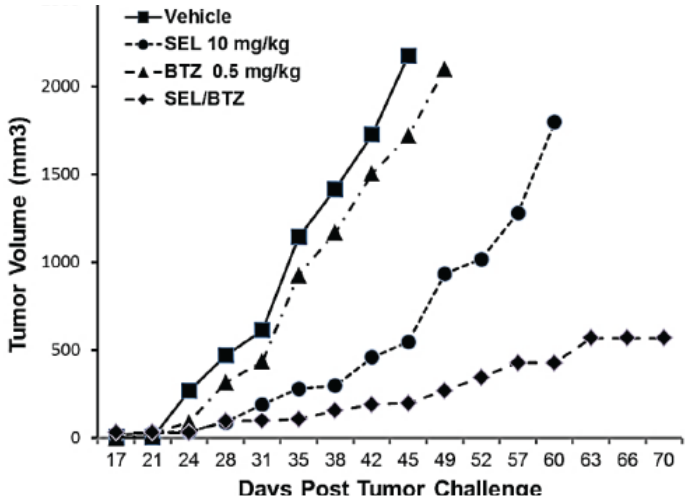


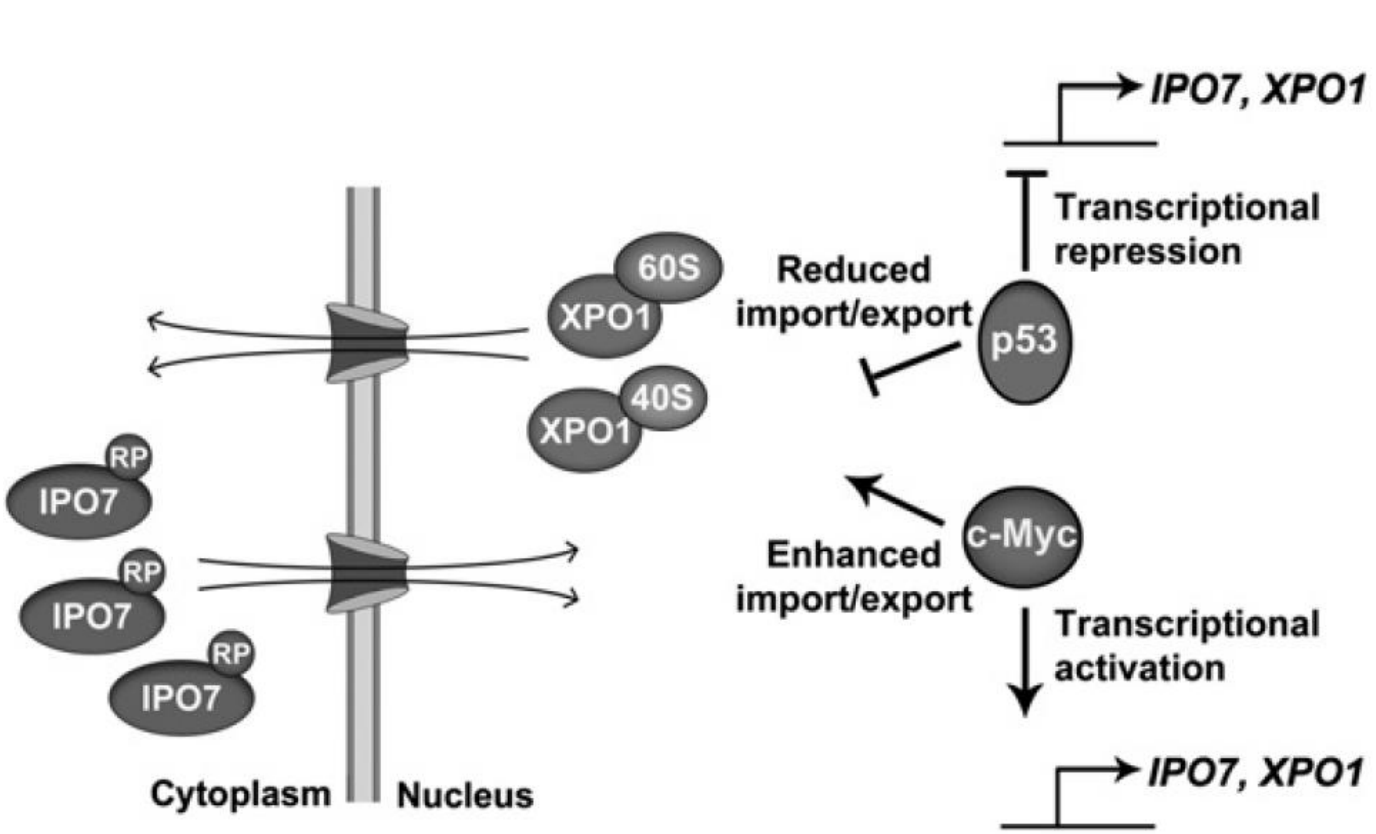


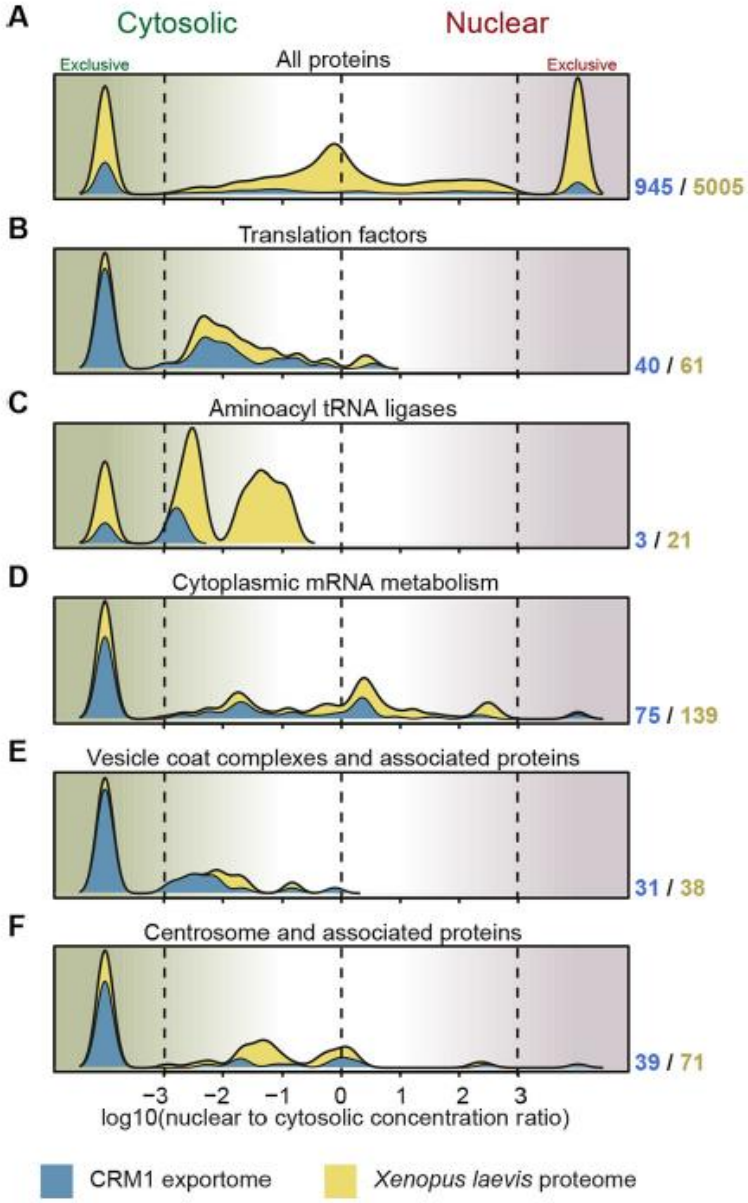


Tiedemann et al Cancer Research 2011
Schmidt et al, Leukemia 2013
Tai et al, Leukemia 2014

Turner et al, Oncotarget 2016
Rosebeck et al, Mol Cancer Ther 2016

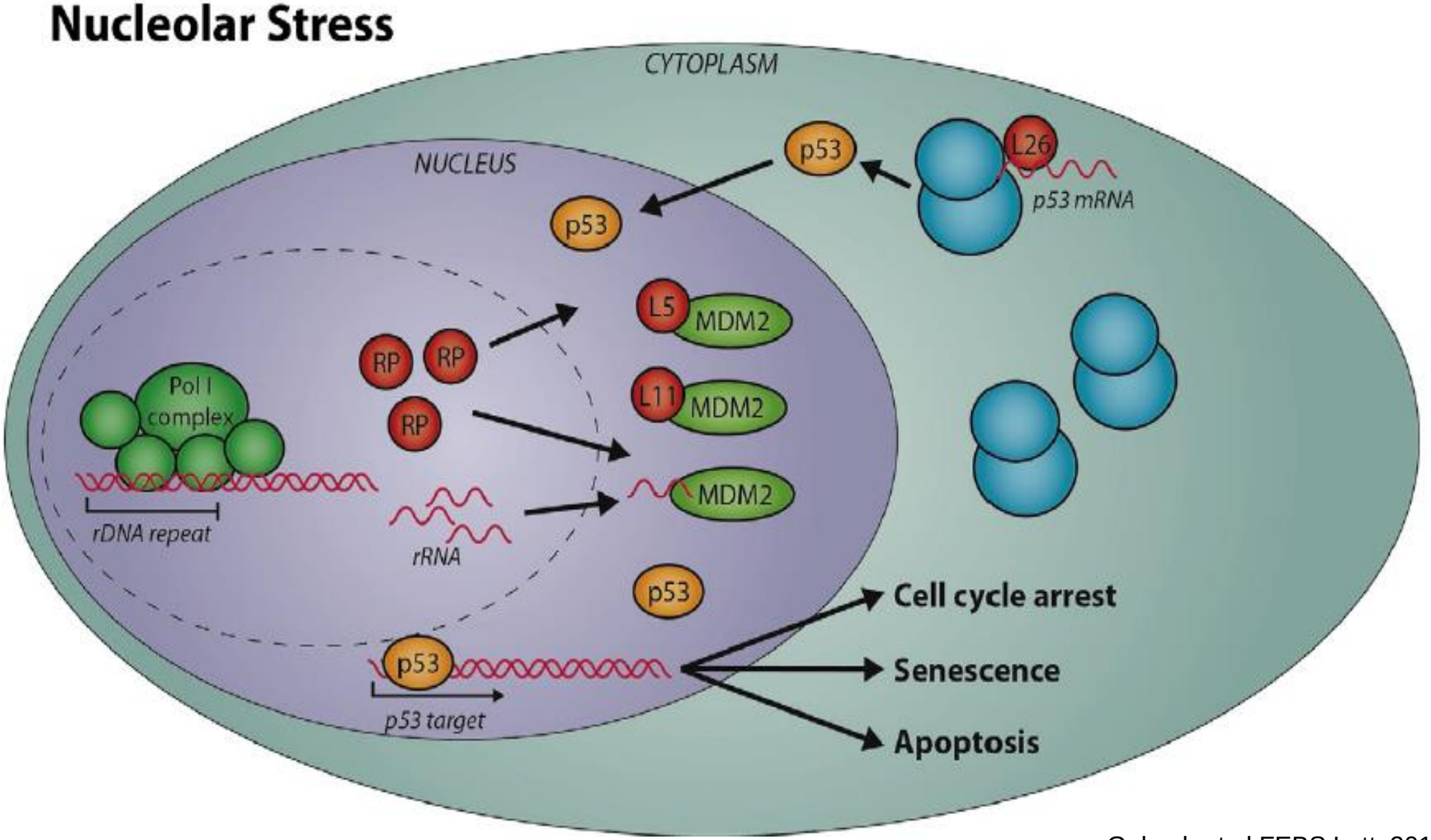
XPO1 regulates translation & Ribosomal biogenesis





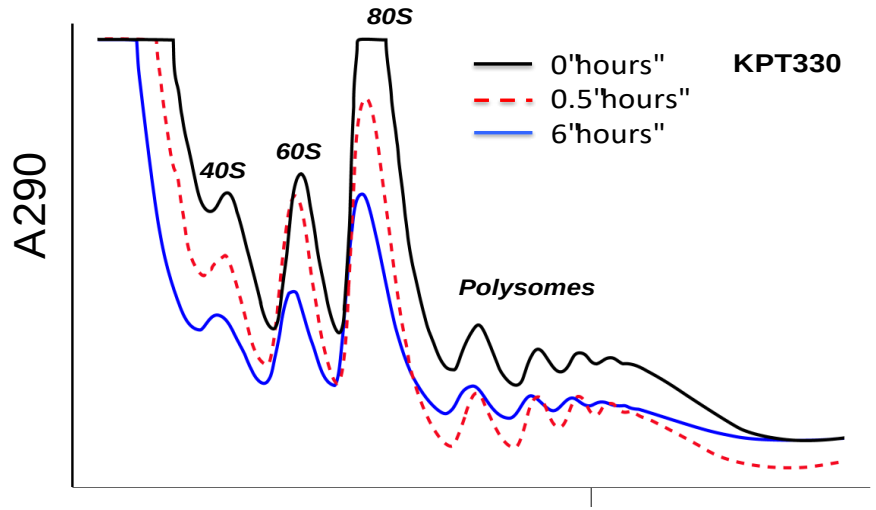
Golomb et al, Molecular Cell 2012
Kirli et al, eLife 2015
Fischer et al, eLife 2015
Moy et al, Genes and Development 1999
Rouquette et al, The EMBO Journal 2005

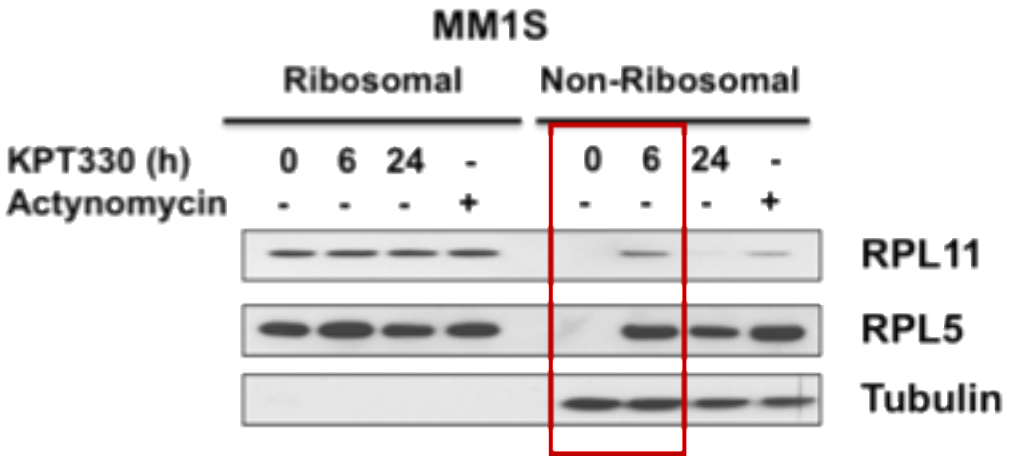
Ribosomal stress response

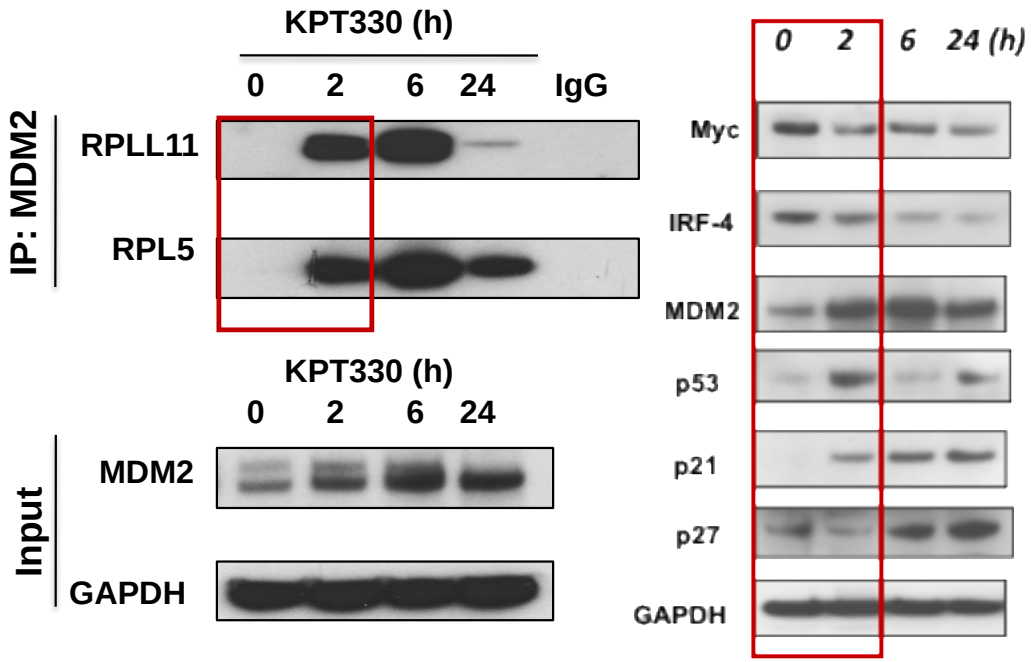


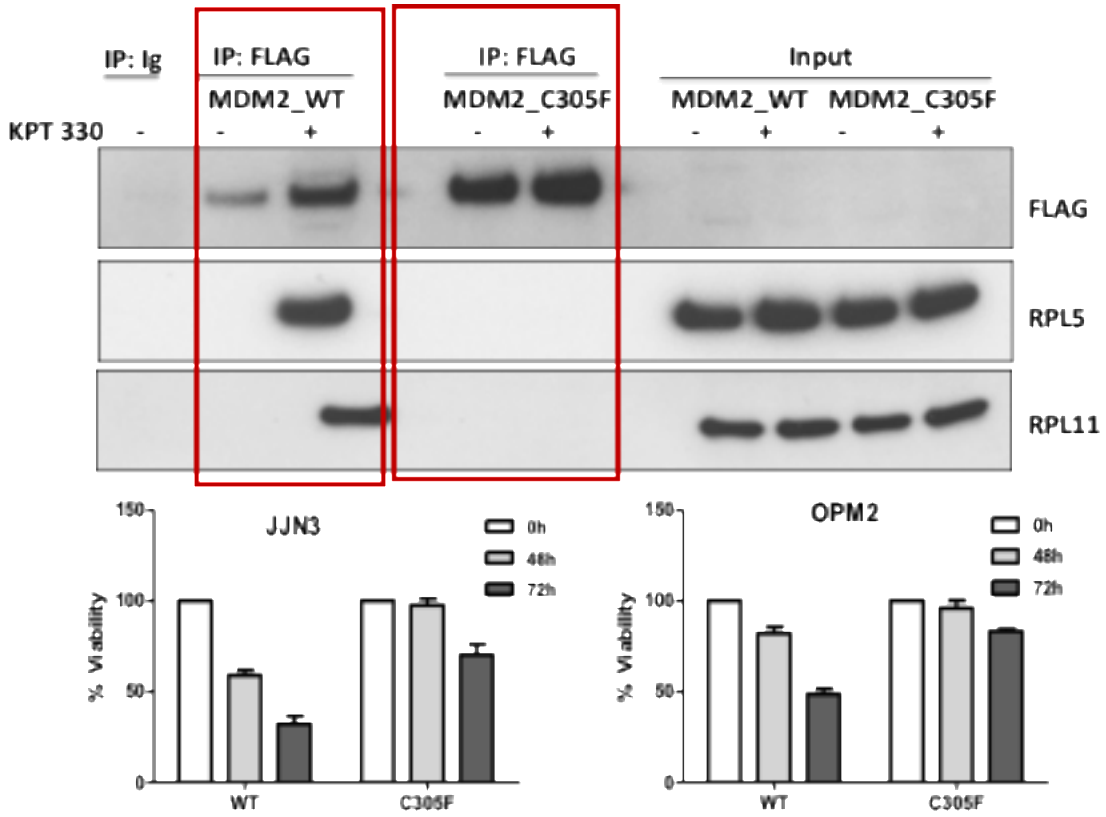
Golomb et al FEBS Lett. 2014
Quin et al Biochimica et Biophysica Acta 2014

XPO1 inhibition induces ribosomal stress response in MM cells



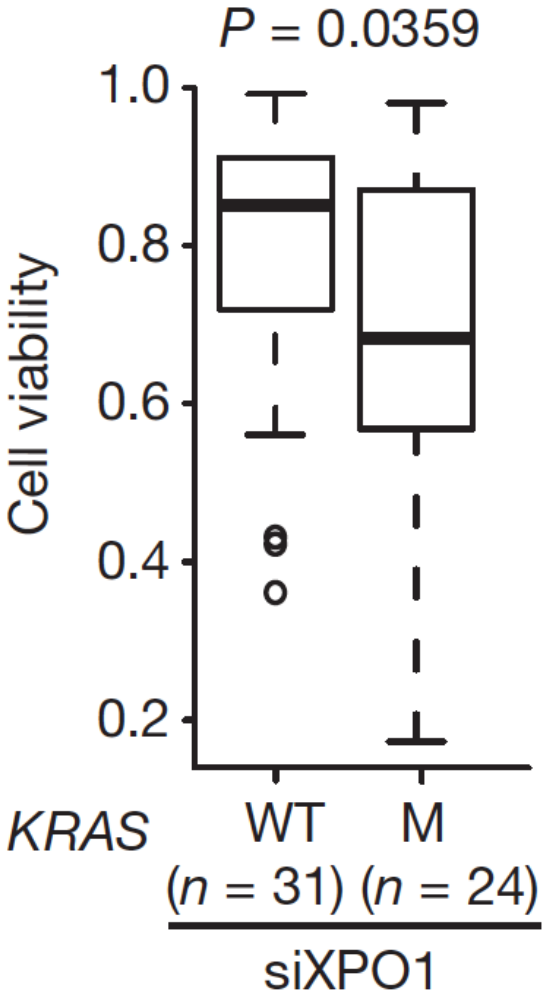


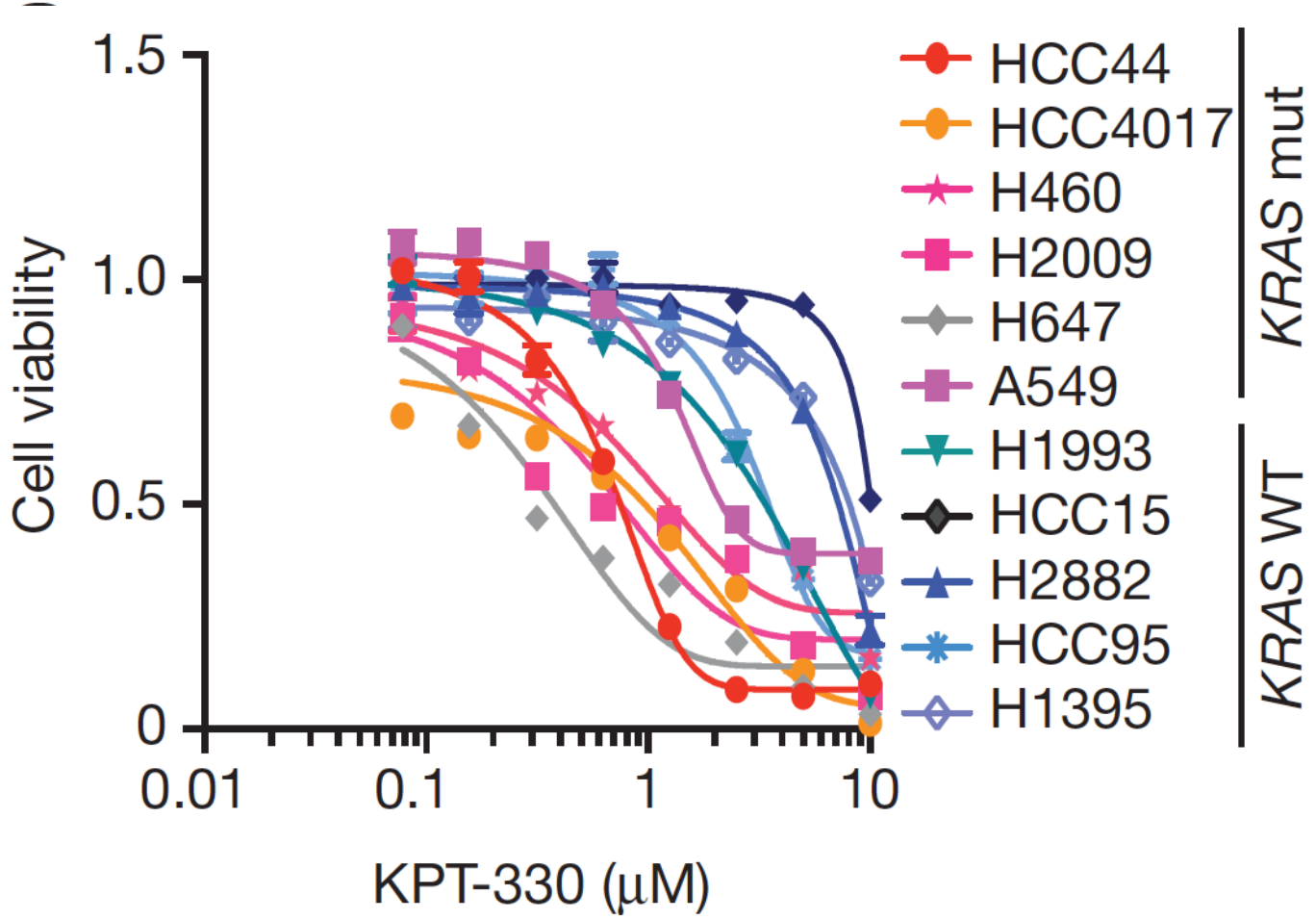




Tagoug I, Bahlis N et al Blood 2014

XPO1-dependent nuclear export is a druggable vulnerability in KRAS-mutant lung cancer





Kim J et al Nature 2016;538: 114–117

Selinexor:
First in Class, Oral Selective Inhibitor of Nuclear Export (SINE)

- XPO1 transports >200 cargo proteins from the nucleus to the cytoplasm
- Overexpression of XPO1, promotes tumor suppressor protein (TSP) mislocalization and proto-oncogene translation

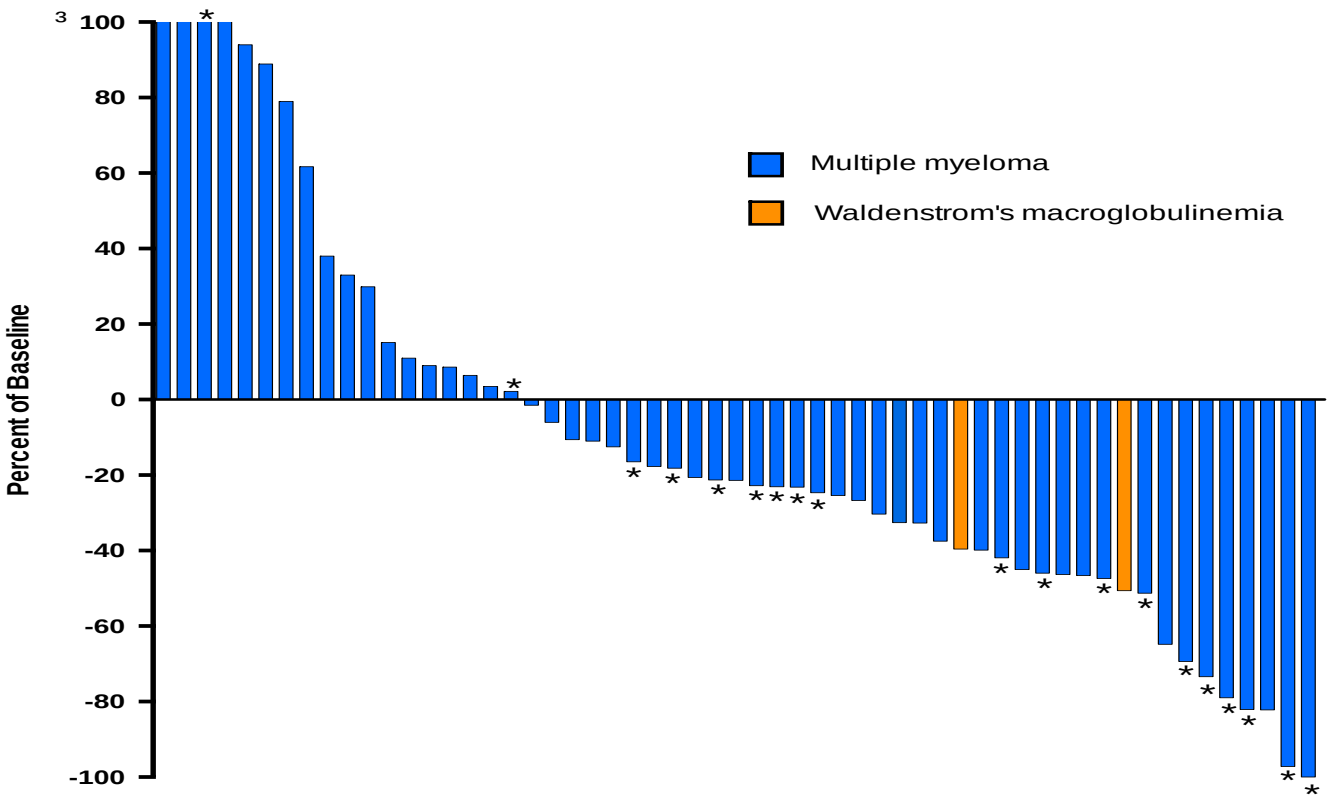
- Selinexor inhibits XPO1 by covalently binding to Cys528 in the cargo pocket, leading to cancer cell death through:
  - **Reactivation of TSPs** (e.g. p53, pRb, IκB, p27, p21, FOXOs)
  - **Inhibition of eIF4E-dependent proto-oncoprotein translation** (e.g. c-Myc, Bcl2, Bcl6, $BclX_L$, cyclins)
  - **Dexamethasone-dependent-reactivation of the glucocorticoid signaling and blocking mTOR pathway**
  - **Disruption of ribosome assembly and induction of ribosomal stress response**

Selinexor + Dexamethasone: Phase 1 Clinical Data in Relapsed Refractory MM

Phase 1 Clinical Trial of Selinexor

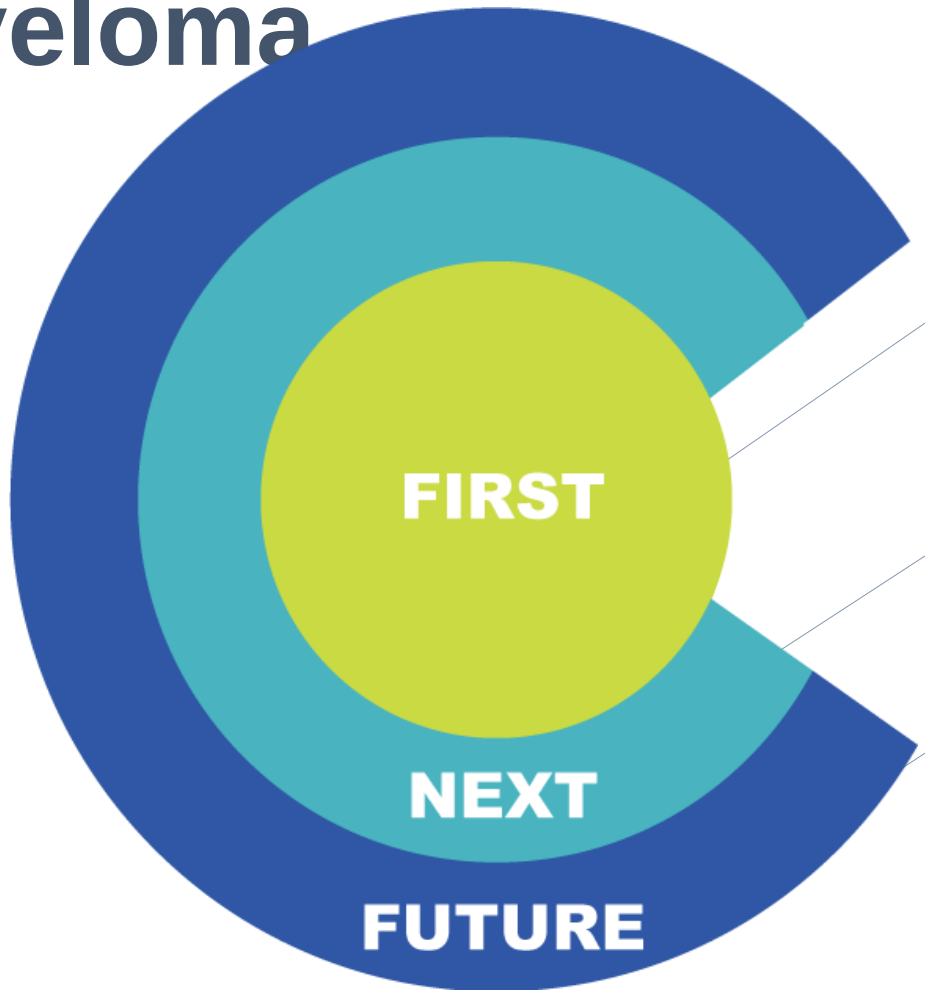
(Chen et al, Blood 2018)

- Enrolled patients with heavily pretreated MM (n=81) or WM (n=3)
- R2PD was selinexor 45 mg/m^2 (~80 mg) and dex (20 mg) given twice weekly
- The combination demonstrated an ORR of 50% at the RP2D (n=12 patients)



∗ Indicates patients treated with selinexor + dexamethasone

Selinexor Development Strategy in Multiple Myeloma



Phase 2b STORM study[1] in penta-refractory[2] myeloma

- Disease refractory to PIs, IMiDs and Darzalex®

Pivotal Phase 3 BOSTON (MCRN 005) study addressing patients with relapsed or refractory disease following 1-3 therapies

- Selinexor and Velcade® *both once weekly*

Phase 1b/2 STOMP as a potential backbone therapy in combination with standard approved therapies

- Selinexor and low-dose dexamethasone combined with Revlimid®, Pomalyst®, Velcade®, Kyprolis® or Darzalex®

[1] Evaluating selinexor with low-dose dexamethasone. [2] Patients who have previously received two PIs, Velcade® (bortezomib) and Kyprolis® (carfilzomib), and two IMiDs, Revlimid® (lenalidomide) and Pomalyst® (pomalidomide), and the anti-CD38 monoclonal antibody Darzalex® (daratumumab), and their disease is refractory to at least one PI, at least one IMiD, and Darzalex®, and their most recent therapy.

Pivotal STORM Part II: Study Design

Oral Selinexor 80 mg + Dexamethasone 20 mg

- Selinexor / dexamethasone twice weekly (Days 1 and 3) until Disease Progression

Patient Population:

- MM previously treated with bortezomib, carfilzomib, lenalidomide, pomalidomide, daratumumab, an alkylator, and glucocorticoids.
- Disease documented to be refractory to ≥1 PI, ≥1 IMiD, daratumumab, glucocorticoid and last line of therapy

Primary Endpoint:

Overall Response rate: ORR

Secondary Endpoints:

Duration of Response (DOR),
Clinical benefit rate (CBR),
Overall survival (OS),
Progression free survival (PFS)
Safety

Key Inclusion/Exclusion:

- Creatinine clearance ≥ 20 mL/min
- ANC ≥ 1,000/mm^3,
- Platelets ≥ 75,000/mm^3 (if BM plasma cell > 50%; plt>50,000/mm^3
- Hemoglobin ≥ 8.5 g/dL

Pivotal STORM Part II: Patient Characteristics

	N=122*
Age, years median (range)	65 (40 – 86)
Time from Diagnosis, Years median (range)	6.6 (1.1 – 23.4)
Males : Females	71 M (58%) : 51 F (42%)
Creatinine Clearance < 60 mL/min	40 (32%)
High Risk Cytogenetics: (del17p, t(4;14), t(14;16), 1q21)	65 (53%)
MM Subtype: FLC	35 (29%)
ECOG Performance Status: 0 / 1 / 2 / Unk	30% / 58% / 9% / 2%
Revised International Staging System (R-ISS): I / II / III / Unk	16% / 64% / 19% / <1%

*A total of 123 patients were enrolled, however 1 patient did not meet eligibility criteria, thus was excluded from this analysis

Pivotal STORM Part II: Prior Therapies

	N=122
Median Prior Regimens (range)	**7 (3 – 18)**
Number of Prior Treatment Regimens ≤6 7–8 ≥9	 48 (39%) 38 (31%) 36 (30%)
Prior Treatments -Refractory to PI / IMiD / Daratumumab / Glucocorticoid -Refractory to Carfilzomib/Pomalidomide/Daratumumab -Refractory to 2 PIs / 2 IMiDs / Daratumumab -Stem Cell Transplant - ≥2 Transplants -Intensive Combination Chemotherapy (e.g. DT-PACE) -Daratumumab in Last Prior Regimen -Daratumumab in Combination -CAR-T Cell Therapy	 122 (100%) 117 (96%) 83 (68%) 102 (84%) 29 (28%) 32 (26%) 58 (48%) 86 (70%) 2 (2%)

Pivotal STORM Part II:

Treatment Related Non-Hematological Adverse Events in ≥10% of Patients

Gastrointestinal Disorders	Grade 1	Grade 2	Grade 3	Grade 4	Total (N=122)
Nausea	32 (26.0%)	41 (33.3%)	12 (9.8%)	--	**85 (69.1%)**
Anorexia	19 (15.4%)	41 (33.3%)	4 (3.3%)	--	**64 (52.0%)**
Vomiting	18 (14.6%)	21 (17.1%)	4 (3.3%)	--	**43 (35.0%)**
Diarrhea	21 (17.1%)	12 (9.8%)	8 (6.5%)	--	**41 (33.3%)**
Altered Taste	7 (5.7%)	5 (4.1%)	--	--	**12 (9.8%)**
Constipation	8 (6.5%)	3 (2.4%)	1 (0.8%)	--	**12 (9.8%)**
Constitutional					
Fatigue/Asthenia	16 (13.0%)	42 (34.1%)	28 (22.8%)	--	**86 (69.9%)**
Weight Loss	31 (25.2%)	26 (21.1%)	1 (0.8%)	--	**58 (47.2%)**
Dizziness	10 (8.1%)	3 (2.4%)	--	--	**13 (10.6%)**
Other					
Hyponatremia	18 (14.6%)	--	20 (16.3%)	--	**38 (30.9%)**
Insomnia	8 (6.5%)	3 (2.4%)	2 (1.6%)	--	**13 (10.6%)**
Pneumonia[1]	--	2 (1.6%)	3 (2.4%)	--	**6 (4.9%)**
Sepsis[2]	--	--	--	1 (0.8%)	**2 (1.6%)**

[1]Pneumonia – 1 Grade 5 Event

[2]Sepsis – 1 Grade 5 Event

Safety data cutoff of August 17, 2018; executed on 02-Sept-2018

Pivotal STORM Part II:

Treatment Related Hematological Adverse Events in ≥10% of Patients

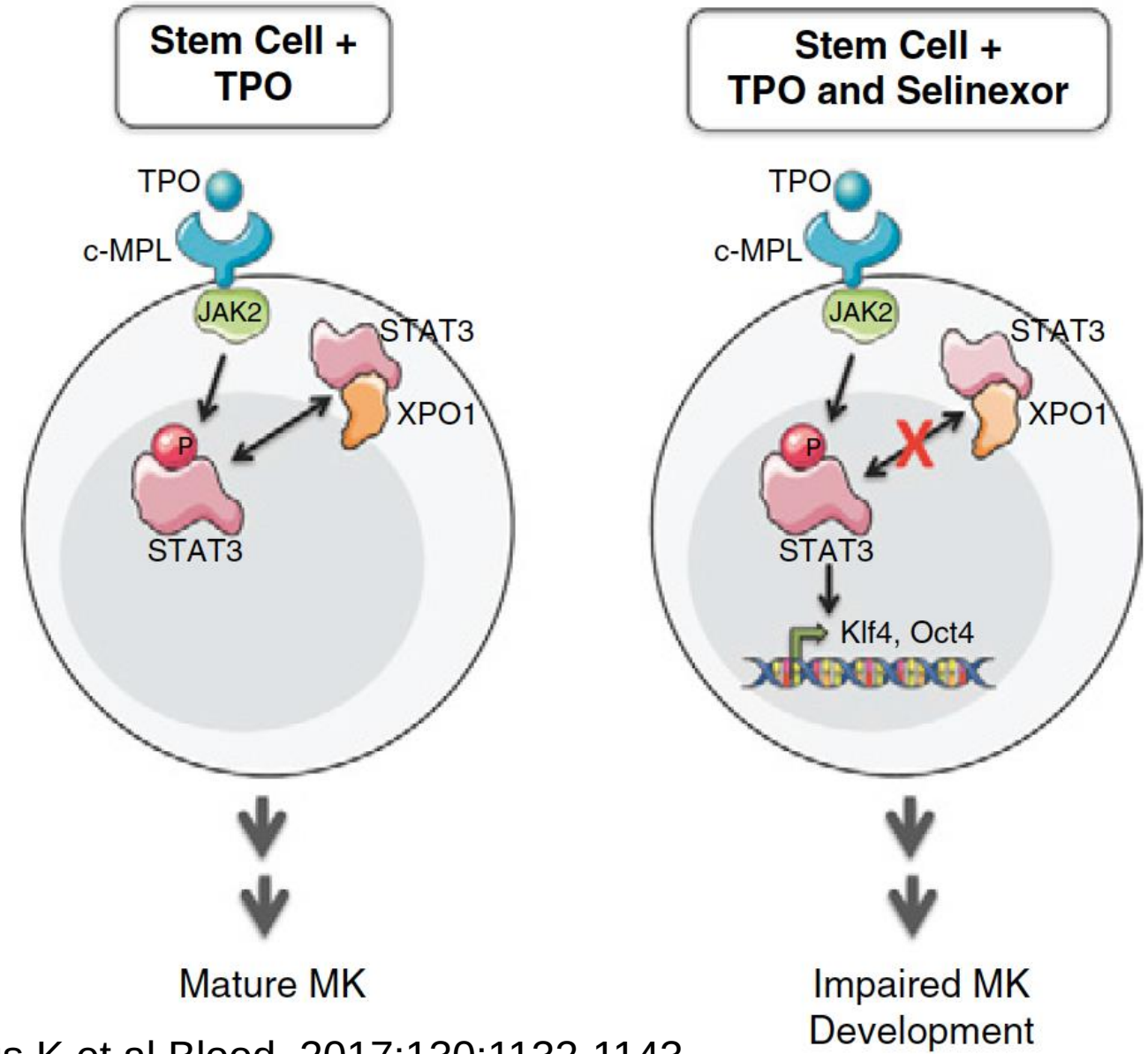
Adverse Event Term	Grade 1	Grade 2	Grade 3	Grade 4	Total (N=122)
Thrombocytopenia	10 (8.1%)	7 (5.7%)	28 (22.8%)	38 (30.9%)	**83 (67.5%)**
Anemia	5 (4.1%)	18 (14.6%)	35 (28.5%)	1 (0.8%)	**59 (48.0%)**
Neutropenia*	6 (4.9%)	16 (13.0%)	18 (14.6%)	4 (3.3%)	**44 (35.8%)**
Leukopenia	6 (4.9%)	13 (10.6%)	17 (13.8%)	--	**36 (29.3%)**
Lymphopenia	2 (1.6%)	4 (3.3%)	8 (6.5%)	3 (2.4%)	**17 (13.8%)**

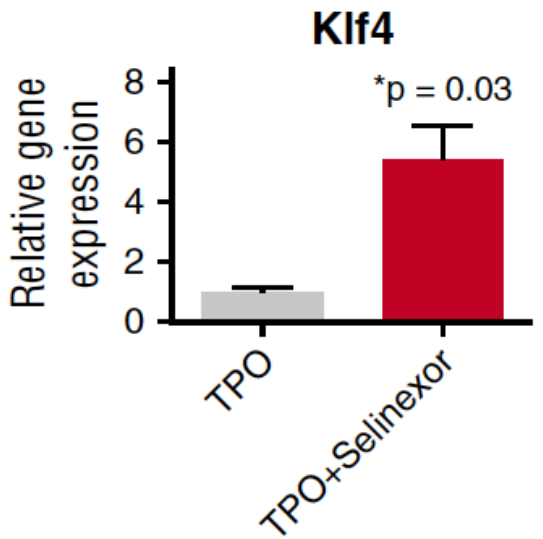
*Febrile Neutropenia (Grade 3) in 2 patients (1.6%)

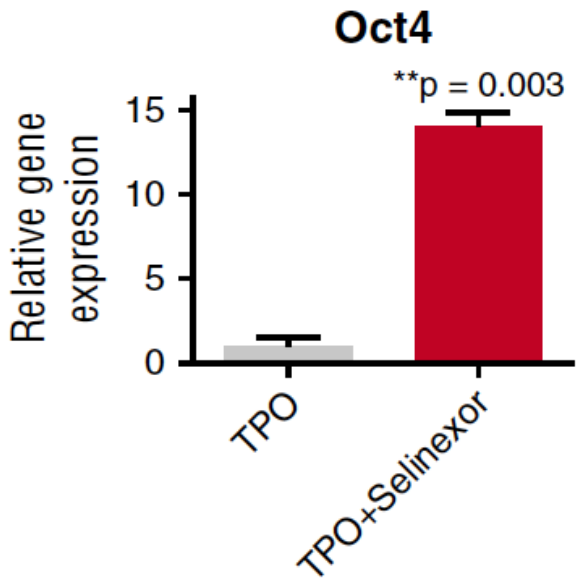
23 patients (19.5%) discontinued due to treatment related AE

Safety data cutoff of August 17, 2018; executed on 02-Sept-2018

Selinexor-induced thrombocytopenia results from inhibition of thrombopoietin signaling in early megakaryopoiesis

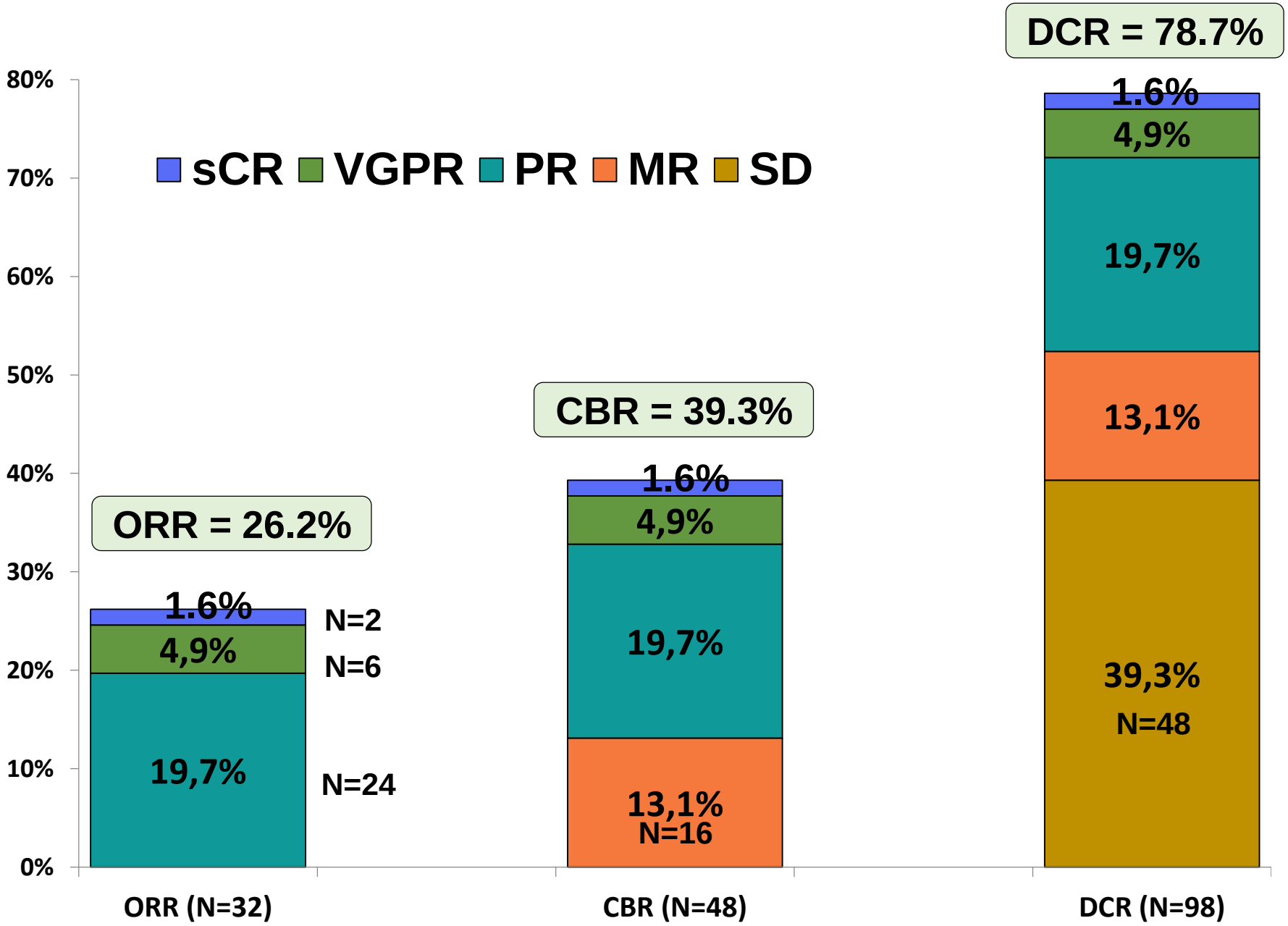






Machlus K et al Blood. 2017;130:1132-1143

Pivotal STORM Part II: Efficacy

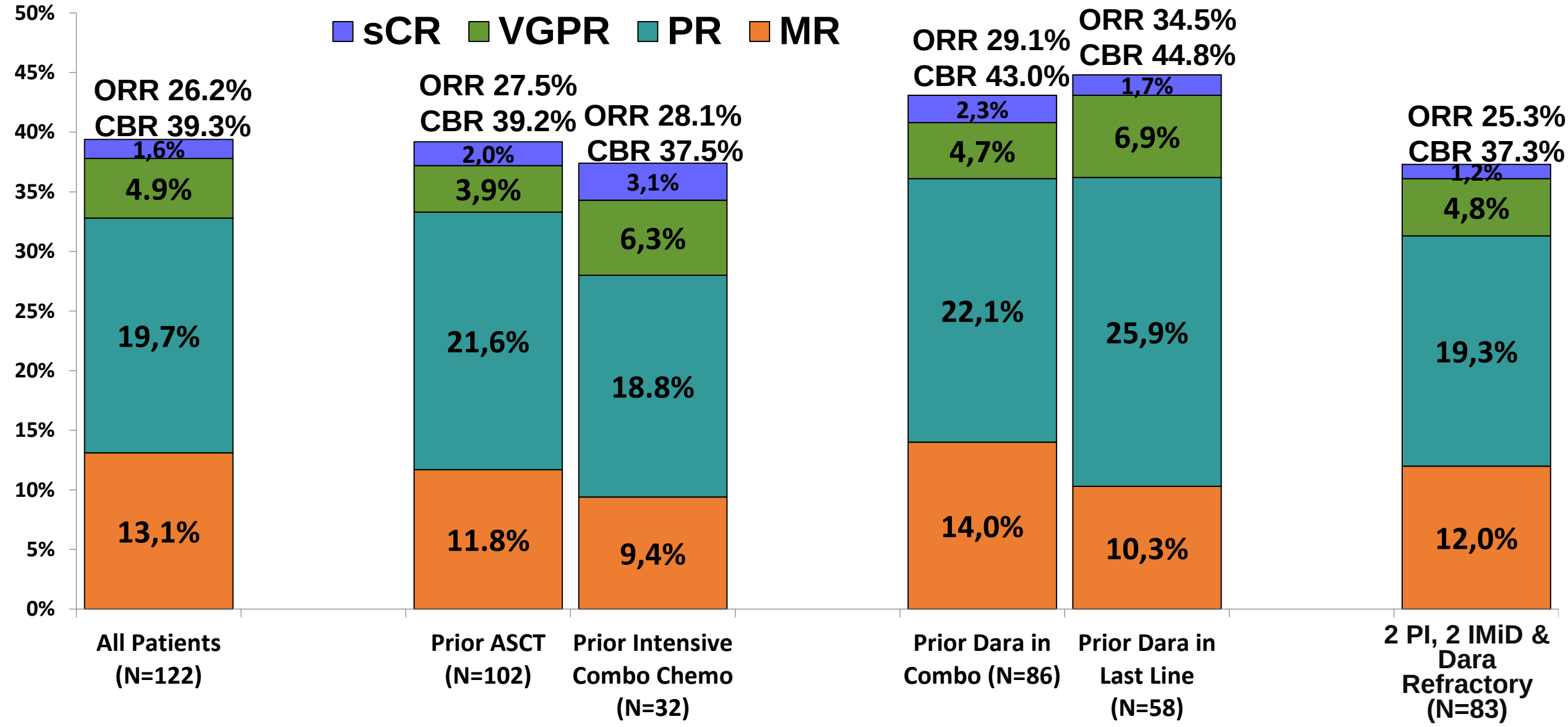


- In penta-refractory MM patients with a median of 7 prior treatment regimens, **ORR of 26.2%,** including **2 stringent CRs /MRD negative** at 10^{-6} and 10^{-4}
- Median time to response was **1 month** (range 1 to 14 weeks)
- 16 patients (13.1%) progressed (PD) on therapy and 10 patients (8.2%) were not evaluable for response

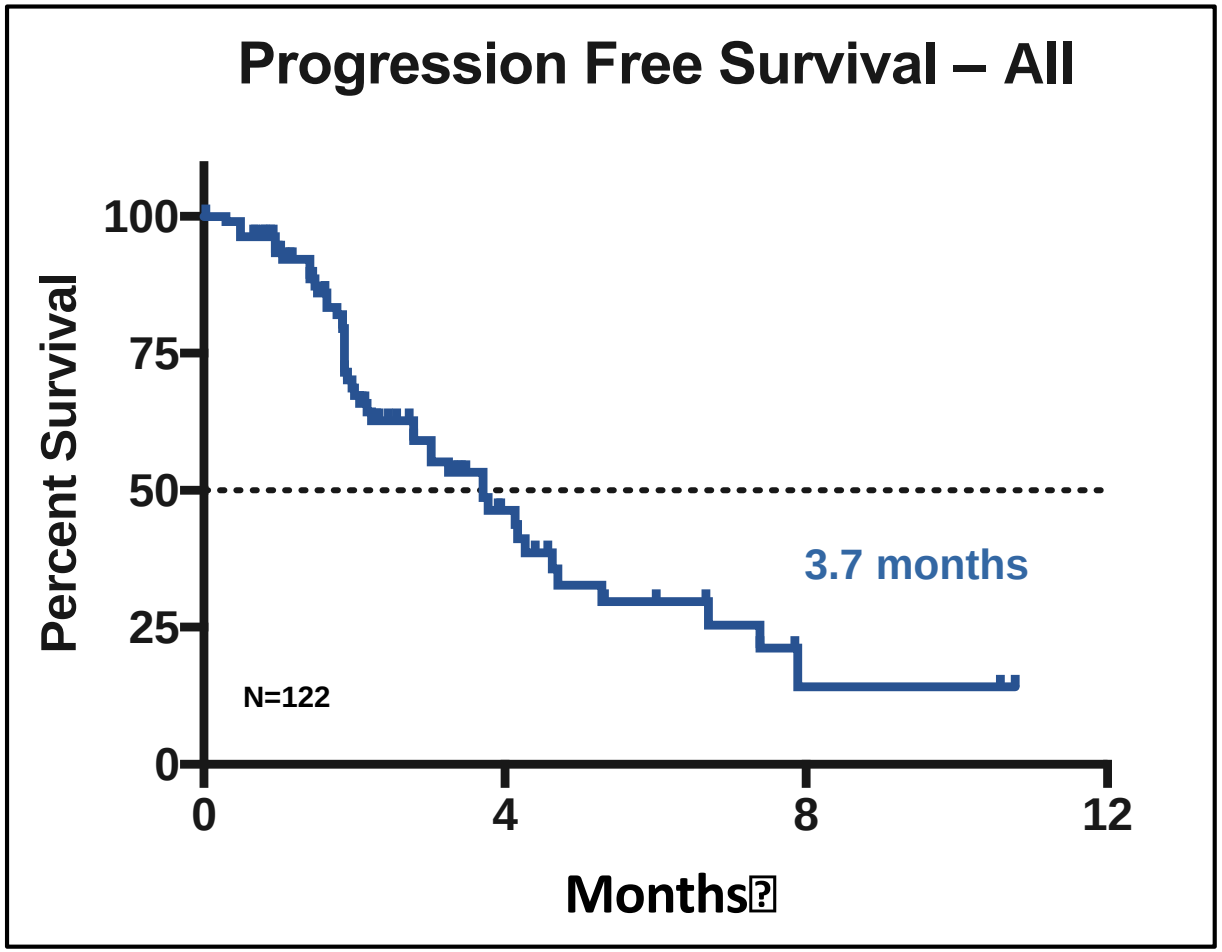
Responses as of August 17, 2018 were adjudicated according to the IMWG criteria *(Kumar, 2016)* by an independent review committee (IRC).

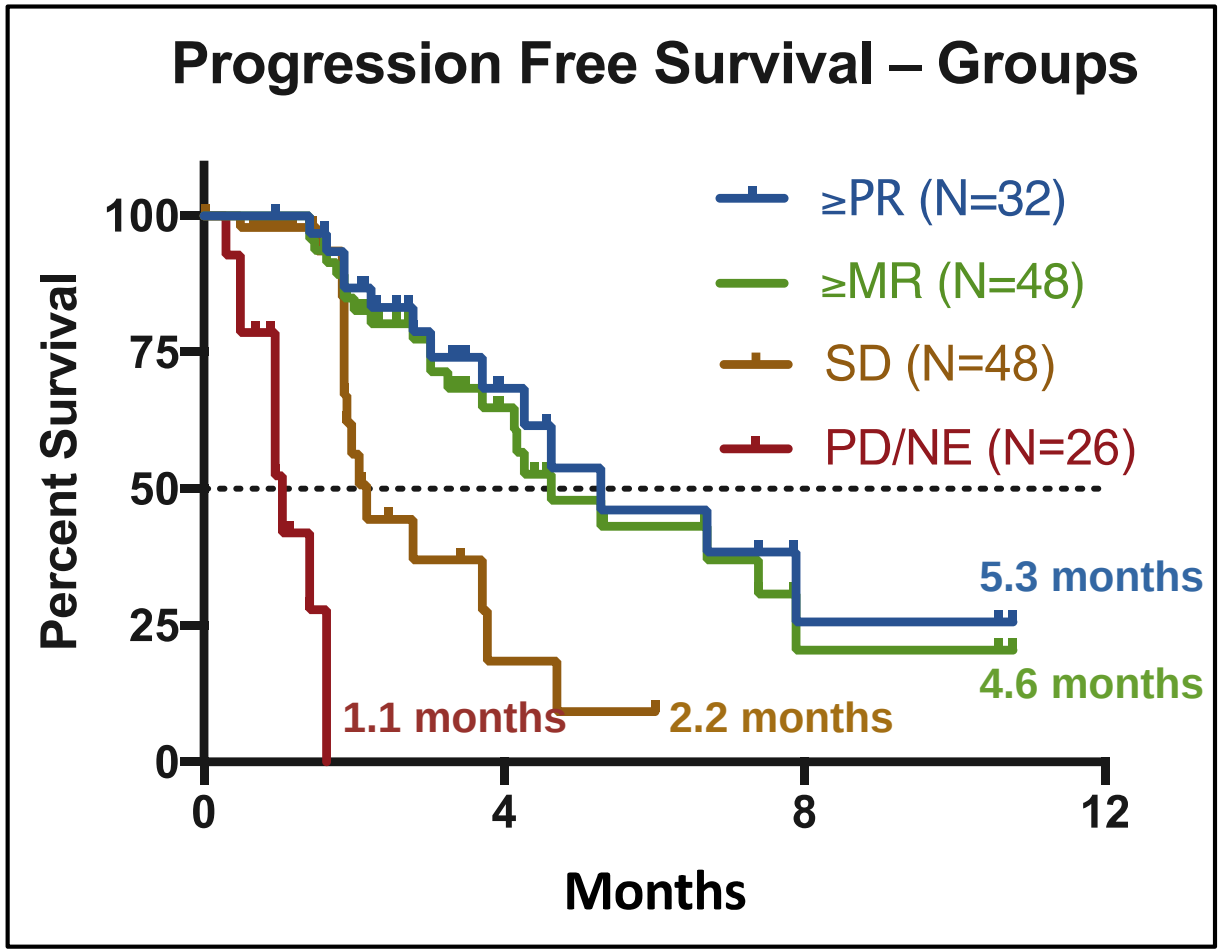
DCR=Disease Control Rate (sCR+VGPR+PR+MR+SD)

Pivotal STORM Part II: Efficacy Sub-Groups



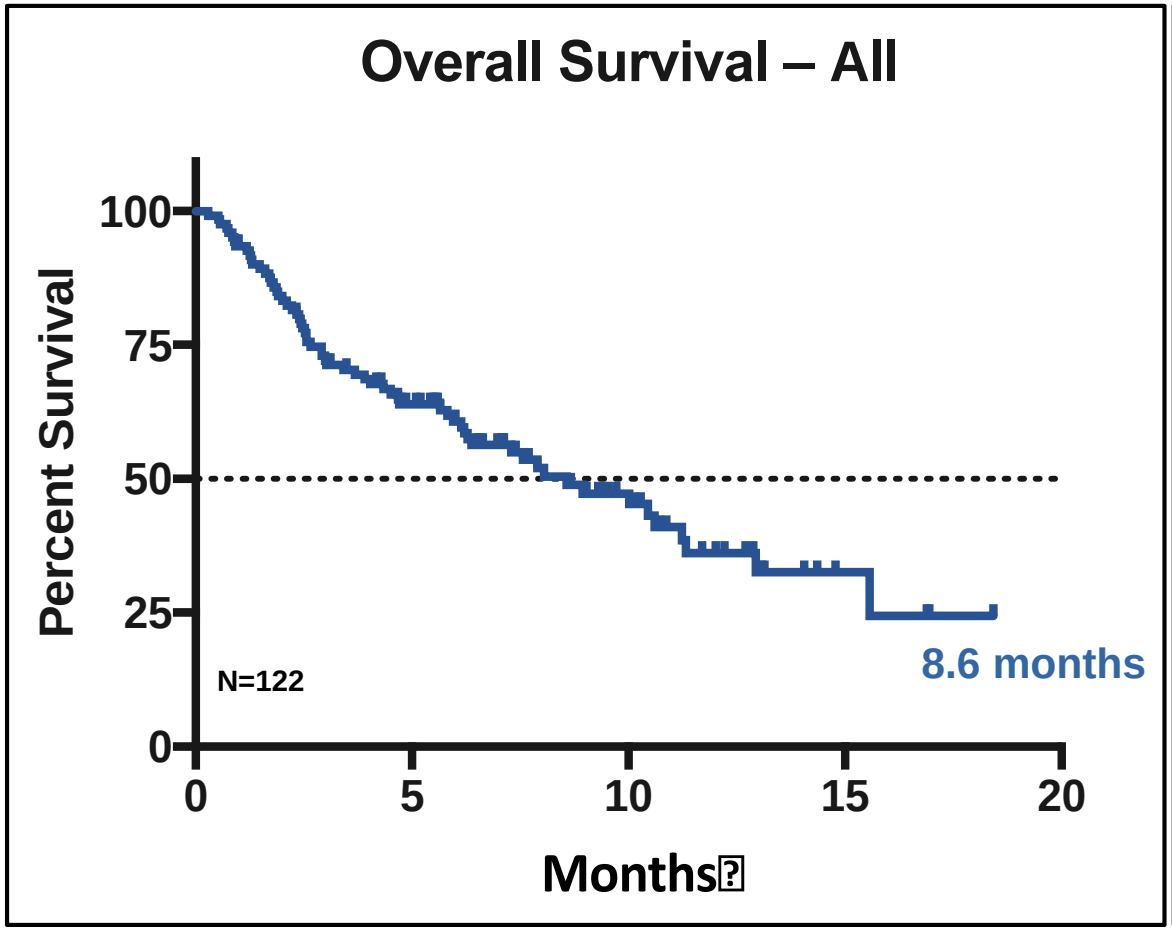
Pivotal STORM Part II: Progression Free Survival

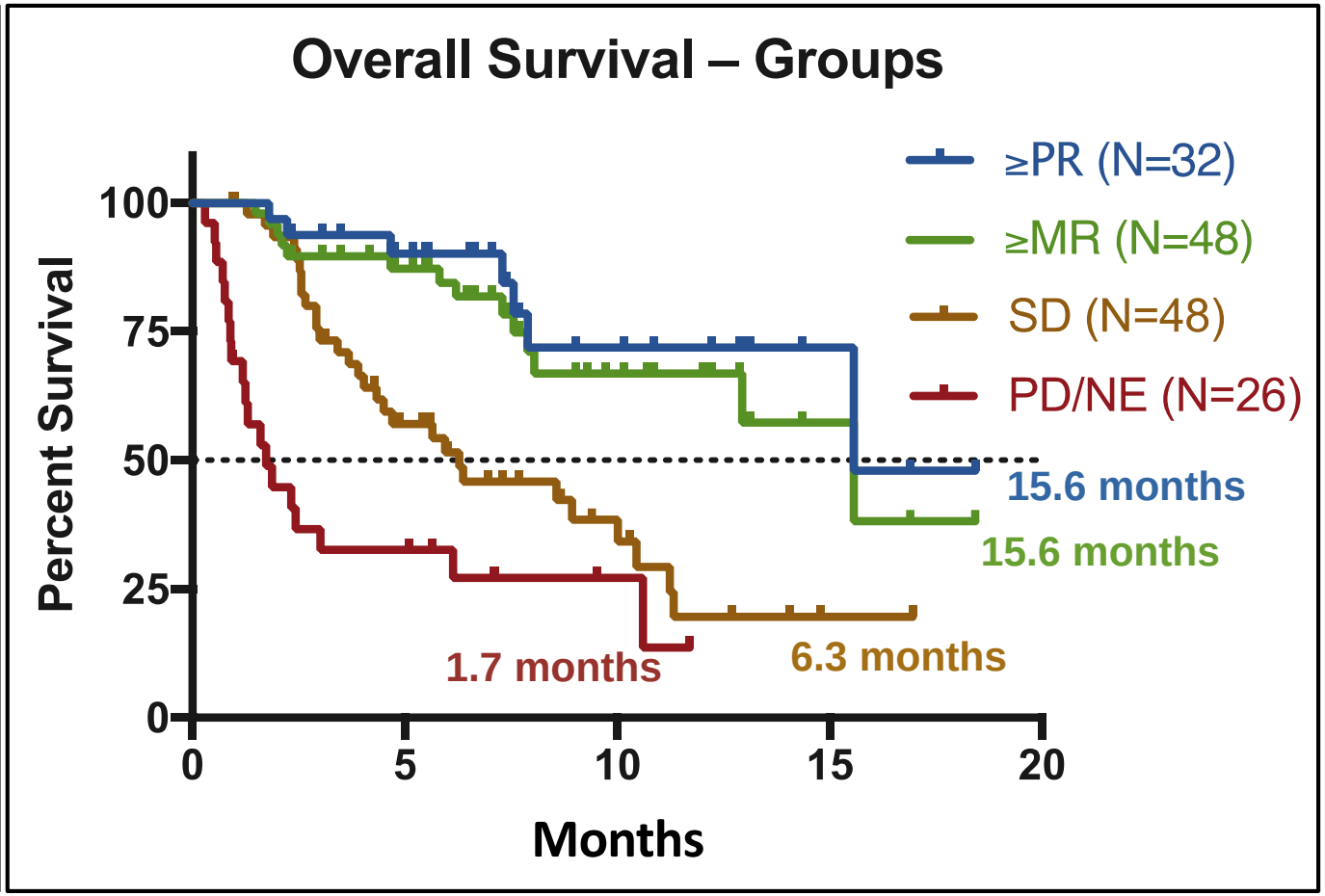




Category	All Patients (N=122)	≥ PR (N=32)	≥ MR (N=48)	SD (N=48)	PD/NE (N=26)
Median PFS	3.7 Months	5.3 Months	4.6 Months	2.2 Months	1.1 Months

Pivotal STORM Part II: Overall Survival





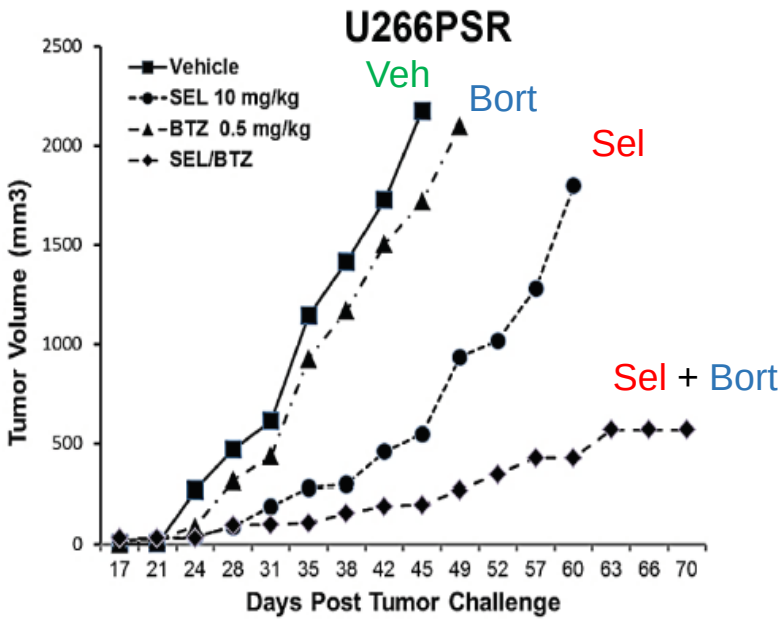
Category	All Patients (N=122)	≥ PR (N=32)	≥ MR (N=48)	SD (N=48)	PD/NE (N=26)
Median OS	8.6 Months	15.6 Months	15.6 Months	6.3 Months	1.7 Months

Pivotal STORM Part II: Conclusions

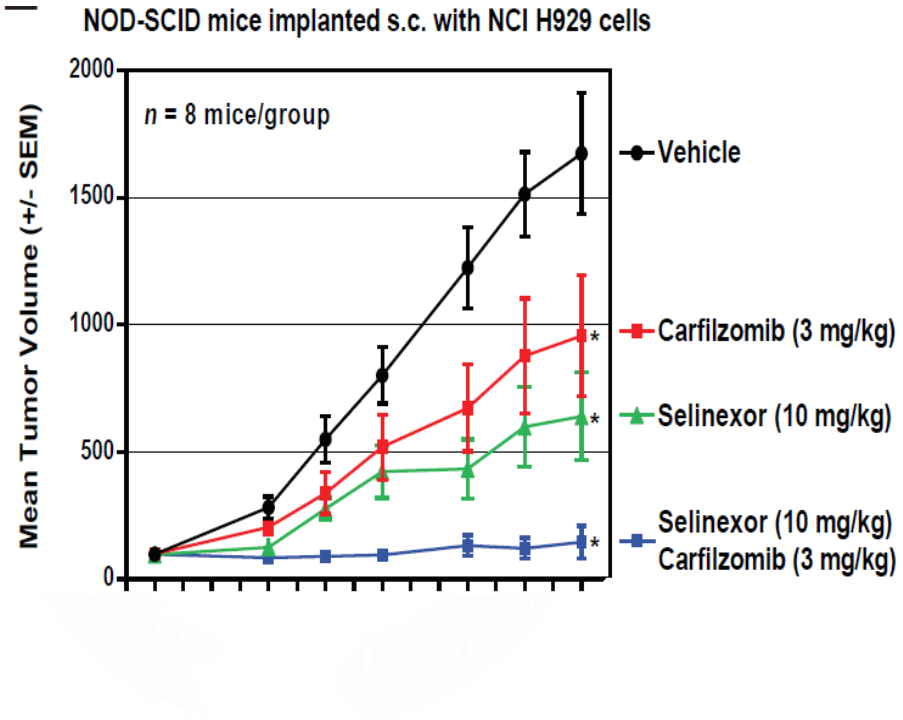
- **Selinexor plus dexamethasone** is an all-oral, first in class investigational treatment with a novel mechanism of action
- Most important G3/4 AEs: thrombocytopenia (53.7%); anemia (29.3%); fatigue (22.8%); hyponatremia (16.3%); nausea (9.8%); diarrhea (6.5%); anorexia (3.3%), emesis (3.3%)
- **Selinexor plus dexamethasone achieved:**
  - **ORR of 26.2% in Penta–Refractory Myeloma**
  - Duration of Response **4.4 months**
  - Clinical Benefit Rate of **39.3%**; Disease Control Rate (≥SD) of **78.7%**
  - 2 patients achieved sCRs: both **MRD negative**
- **Median OS**: **8.6 months**; **15.6 months** in pts that achieved ≥MR; **1.7 months** in pts with PD/NE

Selinexor synergises with anti-MM agents in xenografted Animal Models

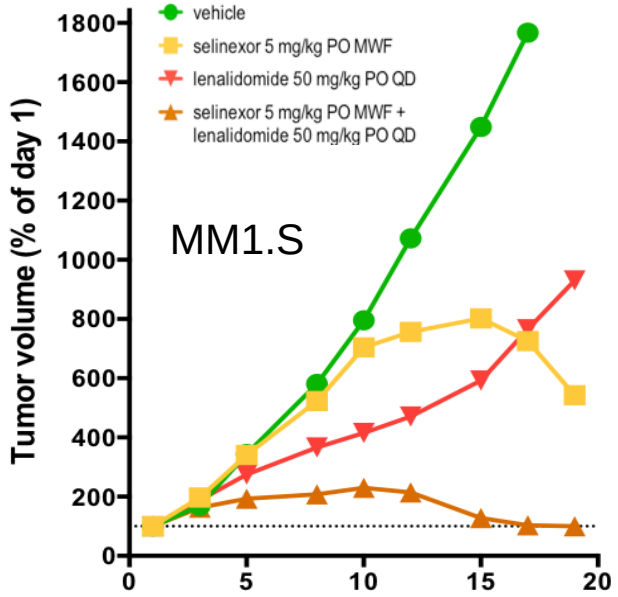
Selinexor + Bortezomib



Selinexor + Carfilzomib



Selinexor + lenalidomide



STOMP: A Phase 1b/2 Study of Selinexor in Combinations In Patients with Multiple Myeloma

Drug	SVd ARM	SPd ARM	SRd ARM	SRd – Newly Diagnosed Patients	SDd ARM	SKd Arm
Selinexor, Oral	60 – 80 mg BIW 80 –100 mg QW	60 – 80 mg BIW 80 – 100 mg QW	60 – 80 mg BIW 80 – 100 mg QW	60 – 80 mg, QW	60 mg BIW 100 mg QW	100 mg QW
Bortezomib, SC	1.3 mg/m^2 – QW/BIW	--	--	--	--	--
Pomalidomide, PO	--	3 – 4 mg, QD	--	--	--	--
Lenalidomide, PO	--	--	25 mg, QD	25 mg, QD	--	--
Daratumumab, IV	--	--	--	--	16 mg/kg, QW	--
Carfilzomib, IV	--	--	--	--	--	56 – 70 mg/m^2, QW
Dexamethasone	20 mg BIW or 40 mg QW	20 mg BIW or 40 mg QW	20 mg BIW or 40 mg QW	20 mg BIW or 40 mg QW	20 mg BIW or 40 mg QW	20 mg BIW or 40 mg QW

Selinexor Combined with Low Dose Bortezomib and Dexamethasone (SVd) Induces a High Response Rate in Patients with Relapsed or Refractory Multiple Myeloma (MM)

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STOMP Study Design

- **S**elinexor and backbone **T**reatments **O**f multiple **M**yeloma **P**atients (**STOMP**) is an open-label, randomized (once- vs. twice-weekly dosing), dose escalation (Phase 1) and expansion (Phase 2) evaluating selinexor plus backbone therapies in patients with relapsed/refractory multiple myeloma (MM)
- **Objectives:**
  - Primary Endpoint: determine MTD and recommended phase 2 dose (RP2D)
  - Secondary Endpoint: determine ORR and DOR for each arm independently
- **Dose Limiting Toxicity (DLT) Definition: Evaluable in Dose Escalation Cycle 1 Only**
  - >1 missed dose (out of 4 doses – once-weekly selinexor dose schedules), or >2 missed doses (out of 6 doses – twice weekly dose schedules) of selinexor during a cycle due to study-drug related toxicity
  - Discontinuation of a patient before completing Cycle 1, due to study-drug related toxicity
  - Grade 3 nausea, vomiting, dehydration, diarrhea or fatigue lasting >3 days despite optimal supportive medications
  - Grade 4 neutropenia lasting > 7 days or Grade ≥ 3 thrombocytopenia with clinically significant bleeding, petechiae or purpura

STOMP Study Design (Cont.)

- **Patient Population SVd**: Patients whose MM has relapsed after ≥ 1 prior therapy – may include prior bortezomib (V), but not refractory to V in their most recent line of therapy
- **SVd Dose Escalation Scheme:** A standard 3 + 3 design will be used for all dose escalations which contains 2 Cohorts to evaluate QW vs. BIW selinexor dosing. V dosing will be evaluated QW vs. BIW. Once the MTD in a cohort is reached, additional patients will be added to determine RP2D.

Drug	SVd ARM	SPd ARM	SRd ARM	SDd ARM	SKd Arm	SRd – Newly Diagnosed Patients
Selinexor, Oral	60 – 80 mg BIW 80 – 100 mg QW	60 – 80 mg BIW 80 – 100 mg QW	60 – 80 mg BIW 80 – 100 mg QW	60 mg BIW 100 mg QW	100 mg QW	60 – 80 mg, QW
Bortezomib, SC	1.3 mg/m^2 – QW/BIW	--	--	--	--	--
Pomalidomide, PO	--	3 – 4 mg, QD	--	--	--	--
Lenalidomide, PO	--	--	25 mg, QD	--	--	25 mg, QD
Daratumumab, IV	--	--	--	16 mg/kg, QW	--	--
Carfilzomib, IV	--	--	--	--	56 – 70 mg/m^2, QW	--
Dexamethasone, Oral	20 mg BIW or 40 mg QW	20 mg BIW or 40 mg QW	20 mg BIW or 40 mg QW	20 mg BIW or 40 mg QW	20 mg BIW or 40 mg QW	20 mg BIW or 40 mg QW

Data presented will focus on the SVd arm. BIW=Twice Weekly, QW=Once Weekly, Dexamethasone will be dosed on selinexor dosing days

SVd Patient Characteristics

SVd Patient Characteristics	N
Enrolled as of June 5, 2018	42
-60 mg selinexor BIW + 1.3 mg/m^2 bortezomib QW	3
-80 mg selinexor BIW + 1.3 mg/m^2 bortezomib QW	6
-80 mg selinexor QW + 1.3 mg/m^2 bortezomib QW	4
-80 mg selinexor QW + 1.3 mg/m^2 bortezomib BIW	3
-100 mg selinexor QW + 1.3 mg/m^2 bortezomib QW (RP2D)	**26**
Median Age, Years (range)	64 (43 – 75)
Males : Females	23 M : 19 F
Median Years from Diagnosis to SVd Treatment, Years (range)	5 (1 – 19)
Median Prior Regimens (range)	**3 (1 – 11)**
-Proteasome Inhibitor Therapy	38 (90%)
-Refractory to Proteasome Inhibitor Therapy	21 (50%)
-Immunomodulatory Drug Therapy	38 (90%)
-Stem Cell Transplant	31 (74%)
International Staging System (ISS) at Diagnosis	
ISS Stage I	16 (38%)
ISS Stage II	11 (26%)
ISS Stage III	11 (26%)
ISS Stage Unknown	4 (10%)

SVd Treatment Related Adverse Events

AE Term	60/80 mg Sel QW/BIW + 1.3 mg/m^2 Bort QW/BIW (N=16)				100 mg Sel QW + 1.3 mg/m^2 Bort QW RP2D Patients (N=26)				Total (N=42)
Hematologic	**Grade 1/2**	**Grade 3**	**Grade 4**	**Total (N=16)**	**Grade 1/2**	**Grade 3**	**Grade 4**	**Total (N=26)**	
Thrombocytopenia	1 (6.3%)	4 (25.0%)	7 (43.8%)	**12 (75.0%)**	1 (3.8%)	3 (11.5%)	5 (19.2%)	**9 (34.6%)**	**21 (50.0%)**
Neutropenia	--	4 (25.0%)	1 (6.3%)	**5 (31.3%)**	1 (3.8%)	6 (23.1%)	--	**7 (26.9%)**	**12 (28.6%)**
Anemia	1 (6.3%)	4 (25.0%)	--	**5 (31.3%)**	3 (11.5%)	1 (3.8%)	--	**4 (15.4%)**	**9 (21.4%)**
Gastrointestinal									
Nausea	5 (31.3%)	2 (12.5%)	--	**7 (43.8%)**	20 (76.9%)	--	--	**20 (76.9%)**	**27 (64.3%)**
Anorexia	8 (50.0%)	1 (6.3%)	--	**9 (56.3%)**	16 (61.5%)	--	--	**16 (61.5%)**	**25 (59.5%)**
Diarrhea	7 (43.8%)	2 (12.5%)	--	**9 (56.3%)**	10 (38.5%)	1 (3.8%)	--	**11 (42.3%)**	**20 (47.6%)**
Vomiting	4 (25.0%)	1 (6.3%)	--	**5 (31.3%)**	8 (30.8%)	--	--	**8 (30.8%)**	**13 (31.0%)**
Altered Taste	2 (12.5%)	--	--	**2 (12.5%)**	4 (15.4%)	--	--	**4 (15.4%)**	**6 (14.3%)**
Constitutional									
Fatigue	9 (56.3%)	--	--	**9 (56.3%)**	10 (38.5%)	6 (23.1%)	--	**16 (61.5%)**	**25 (59.5%)**
Weight loss	5 (31.3%)	--	--	**5 (31.3%)**	5 (19.2%)	--	--	**5 (19.2%)**	**10 (23.8%)**
Dehydration	2 (12.5%)	--	--	**2 (12.5%)**	3 (11.5%)	--	--	**3 (11.5%)**	**5 (11.9%)**
Other									
Vision Blurred	2 (12.5%)	--	--	**2 (12.5%)**	6 (23.1%)	--	--	**6 (23.1%)**	**8 (19.0%)**
Edema	4 (25.0%)	--	--	**4 (25.0%)**	3 (11.5%)	--	--	**3 (11.5%)**	**7 (16.7%)**
Peripheral Neuropathy	2 (12.5%)	--	--	**2 (12.5%)**	4 (15.4%)	--	--	**4 (15.4%)**	**6 (14.3%)**
Cataract	3 (18.8%)	--	1 (6.3%)	**4 (25.0%)**	2 (7.7%)	--	--	**2 (7.7%)**	**6 (14.3%)**
Confusion	1 (6.3%)	1 (6.3%)	--	**2 (12.5%)**	3 (11.5%)	--	--	**3 (11.5%)**	**5 (11.9%)**
Hyponatremia	2 (12.5%)	--	--	**2 (12.5%)**	1 (3.8%)	2 (7.7%)	--	**3 (11.5%)**	**5 (11.9%)**

Treatment Related Adverse Events as of June 5th, 2018

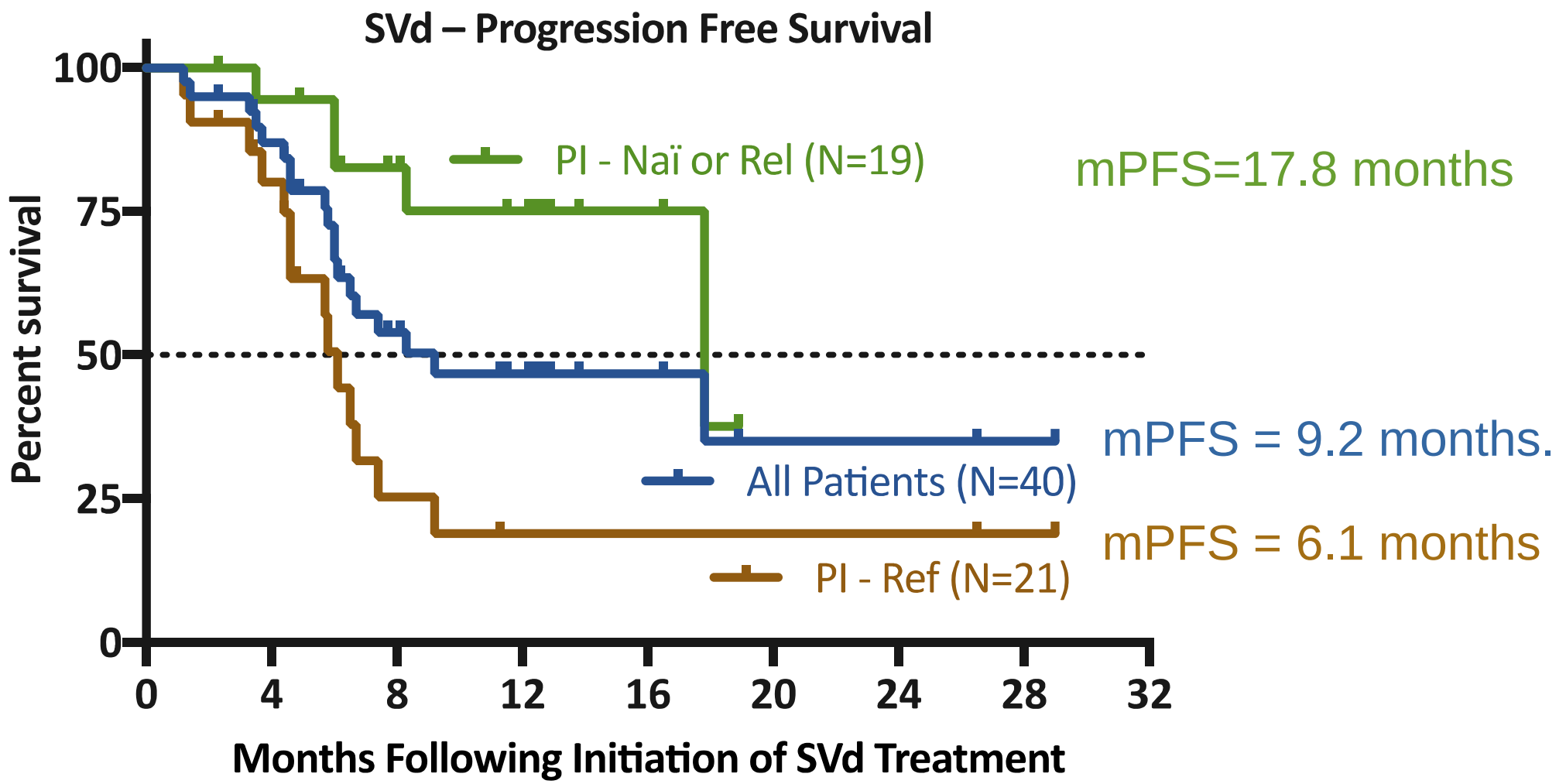
- MTD was not reached. No DLT's were reported.
- Patients (n=3)in the BIW bortezomib (V) cohort were reduced to QW after C1.
- No G3 eripheral neuropathy, G2: 2 patients.
- RP2D of SVd is Sel 100 mg, V 1.3 mg/m^2 and dex 40 mg, QW

SVd Efficacy

Best Responses† in Evaluable SVd Patients as of June 5th, 2018										
Category	**N***	**ORR**	**CBR**	**sCR**	**CR**	**VGPR**	**PR‡**	**MR**	**SD**	**PD**
PI Relapsed or Naïve	19	**84%**	**95%**	5%	16%	16%	47%	11%	5%	--
PI Refractory	21	**43%**	**67%**	--	5%	19%	19%	24%	29%	5%
PI Relapsed or Naïve, ≤ 3 Prior Treatments (BOSTON)**	18	**83%**	**89%**	6%	17%	22%	39%	6%	11%	--

†Responses were adjudicated according to the *International Myeloma Working Group* criteria, **two patients not evaluable for response: one death unrelated to myeloma and one withdrawal of consent before disease follow up.* ‡one unconfirmed PR. ORR=Overall Response Rate (sCR+CR+VGPR+PR), sCR=Stringent Complete Response, CR=Complete Response, VGPR=Very Good Partial Response, PR=Partial Response, MR=Minor Response, SD=Stable Disease, PD=Progressive Disease, CBR=Clinical Benefit Rate (ORR+MR). Responses as of June 5th, 2018 based on interim unaudited data. **BOSTON: patient population eligible for the ongoing Phase 3 Randomized BOSTON Study of SVd versus Vd.

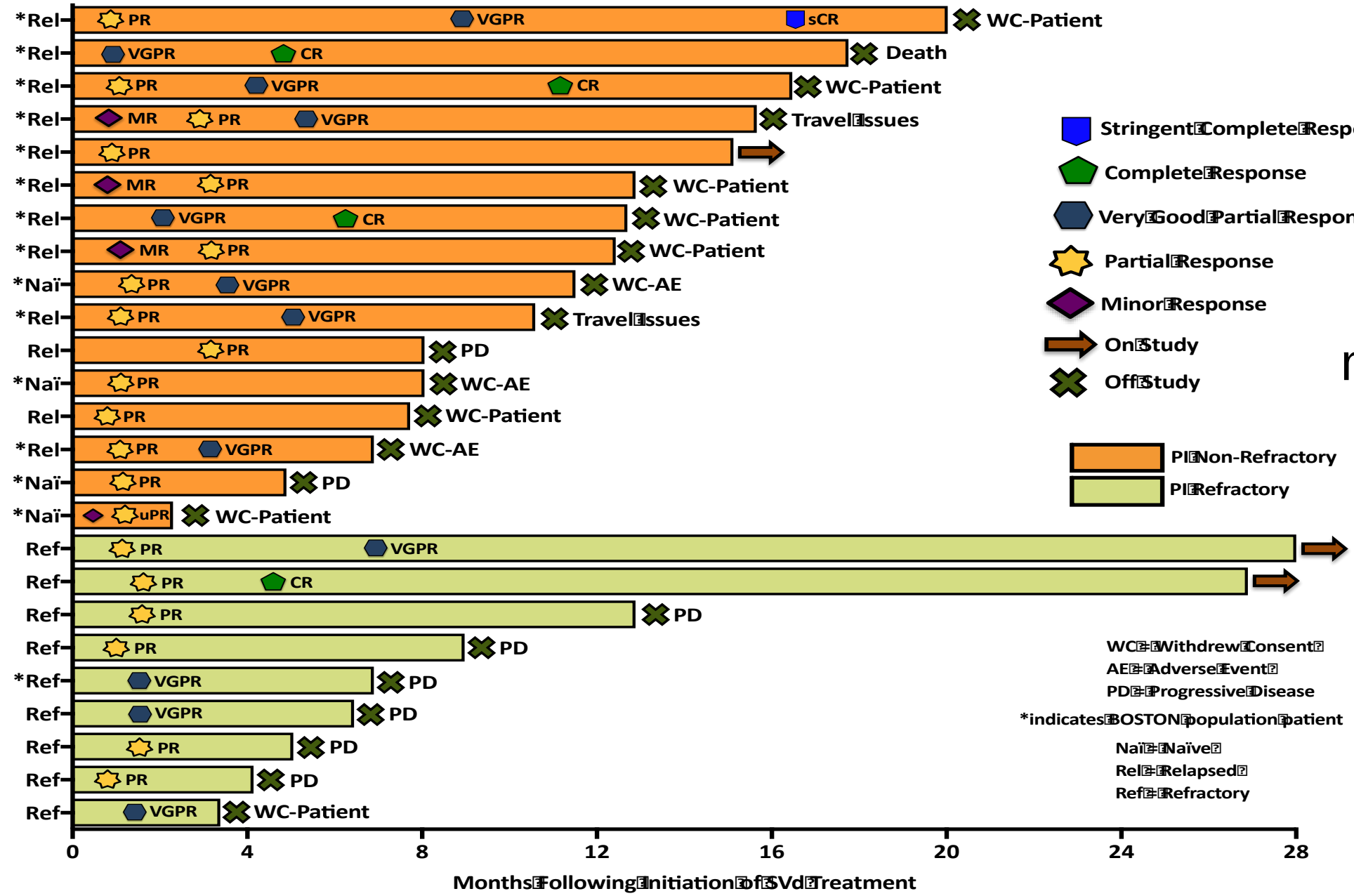
SVd Progression Free Survival (PFS)



Patients at Risk

Months	0	3.7	4.9	6.1	8.3	12.2	13.8	16.5	18.9	26.5	29
All Patients	40	33	27	22	15	11	6	5	3	2	1
PI Naï or Rel	19	18	17	16	11	9	4	3	1	--	--
PI Ref	21	16	11	8	5	3	--	--	--	2	1

SVd induces durable responses



mDOR =13 months

Summary and Conclusions

- **SVD Most common AEs: anorexia, nausea, fatigue (G1-2), and thrombocytopenia**

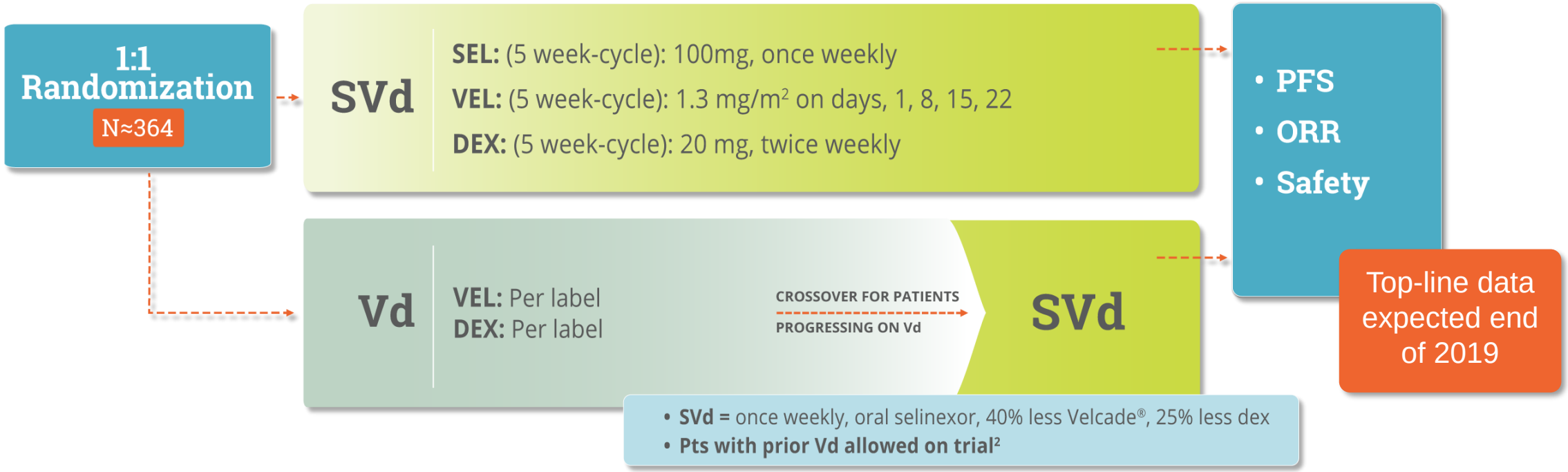
- **ORR of 84% in patients with PI relapsed or naïve MM**
- **ORR of 43% in patients with PI refractory MM**

- **The PFS is 17.8 months in patients with PI naïve or relapsed MM**

- **RP2D of SVd: Selinexor 100 mg, V 1.3 mg/m^2 and deX 40 mg, once-weekly (35 day cycle)**

- **The high ORR rate and PFS of 17.8 months in patients with ≤ 3 prior therapies treated with SVd support the ongoing Phase 3 BOSTON study examining SVd vs Vd**

BOSTON[1]: A Phase 3 Study In Myeloma



Ongoing randomized, open-label clinical trial evaluating *once weekly* selinexor and Velcade® (bortezomib) plus low-dose dex versus standard *twice-weekly* Velcade® plus low-dose dex in patients with relapsed or refractory MM, who have had 1-3 prior lines of therapy

[1] Bortezomib, Selinexor and dexamethasone [2] Pts must have achieved ≥PR, and completed proteasome inhibitor therapy at least 60 days prior.