23rd Congress of the European Hematology Association
14-17 June 2018
Stockholm, Sweden

INTERIM UPDATE FROM A PHASE 2 MULTICENTER STUDY OF TAZEMETOSTAT, AN EZH2 INHIBITOR, IN PATIENTS WITH RELAPSED OR REFRACTORY FOLLICULAR LYMPHOMA

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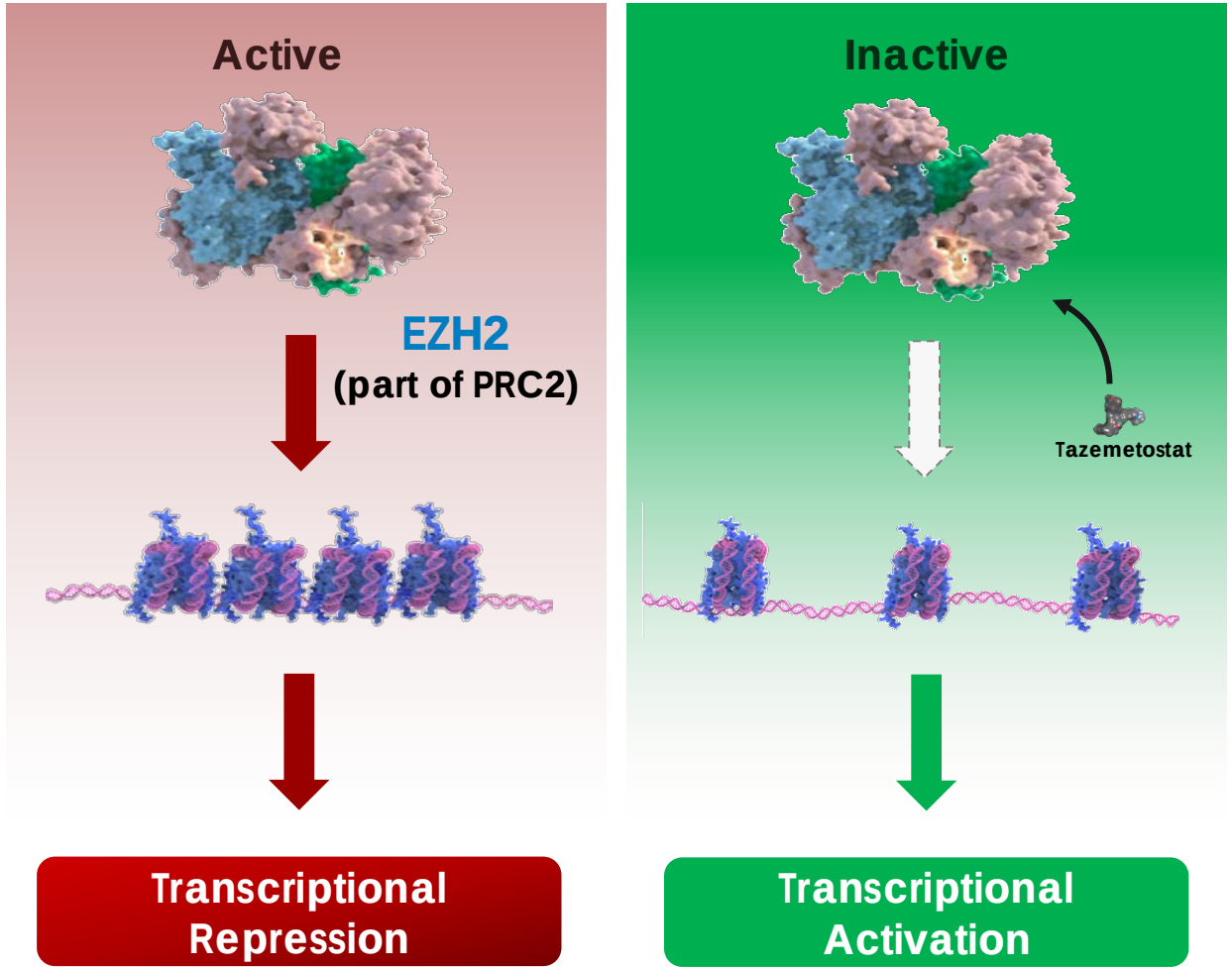
SPEAKER DISCLOSURE

- Dr Gilles Salles has received honoraria from Roche, Janssen, Gilead, Celgene, Novartis, Amgen, Merck, Servier, and Epizyme

TAZEMETOSTAT FOR THE TREATMENT OF B-CELL NHL

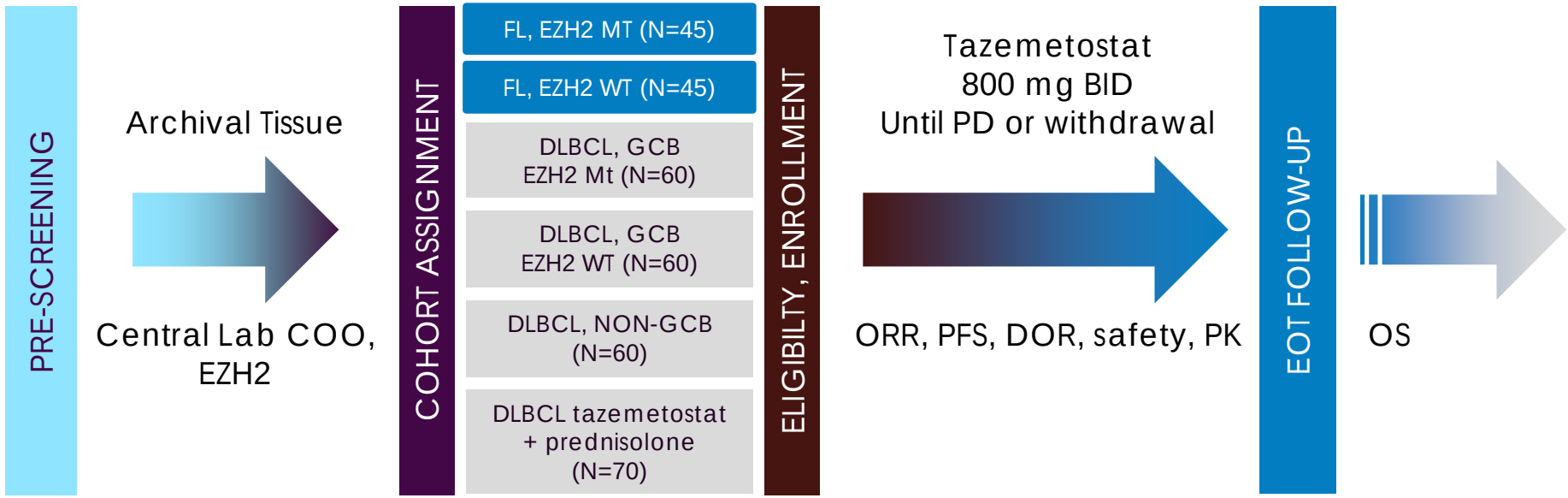
- EZH2 is an epigenetic regulator of gene expression and plays a critical role in multiple forms of cancer
  - Activating mutations of *EZH2* can act as an oncogenic driver, especially in FL and GCB-DLBCL, and is present in ~20% of patients
- Tazemetostat
  - First-in-class, potent, selective, reversible oral inhibitor of mutated and wild-type EZH2
  - Preclinical activity in DLBCL cells lines, with greater activity in EZH2 mutant models
  - Monotherapy activity and favorable safety in phase 1/2 studies in patients with relapsed or refractory (R/R) NHL, as well as certain genetically defined solid tumors[1]



1. Italiano A, et al. *Lancet Oncol*. 2018;19(5):649-659.

TAZEMETOSTAT PHASE 2 NHL STUDY DESIGN

- Global, multi-center, open-label study in 6 cohorts of patients with R/R FL or DLBCL
  - Patients prospectively assigned to cohorts according to *EZH2* mutational status
    - **cobas**® *EZH2* Mutation Test (in development, Roche Molecular Systems)
  - ≥2 prior therapies
- Primary endpoint: objective response rate (ORR)
  - Secondary efficacy endpoints: progression-free survival (PFS), duration of response (DOR), safety and tolerability
  - Objective response assessed by IWG-NHL criteria (Cheson 2007)
    - Restaging every 8 weeks for 6 cycles, then every 12 weeks thereafter



PHASE 2 NHL STUDY PROGRESS; FL COHORTS

- **Data cut-off:** May 1, 2018
- **Safety:** 82 patients
- **Efficacy:**
  - FL wild-type *EZH2* – 54 evaluable for efficacy
    - Closed to accrual
  - FL mutated *EZH2* – 28 evaluable for efficacy
    - Open to accrual

FL DEMOGRAPHICS AND DISEASE CHARACTERISTICS

Characteristic	EZH2 Status	
	Mutant (n=28)	Wild-type (n=54)
Median age, years	61	61
Males, %	43	63
ECOG PS 0-1, %	96	93
B symptoms, n (%)	2 (7)	10 (19)
Median tumor burden[a], mm^2 (range)	2969 (162-16543)	2948 (128-29819)
Prior lines of therapy, n (%)		
1	1 (4)	0
2	2 (43)	17 (31)
3	6 (21)	10 (19)
4	3 (11)	11 (20)
≥ 5	5 (18)	16 (30)
median	3	4
Refractory to last regimen[b], n (%)	10 (38)	22 (42)
Prior HSCT, %	11	39
Median time from initial diagnosis, years	5.1	6.4
Median time from last prior therapy, weeks	18.4	28.1

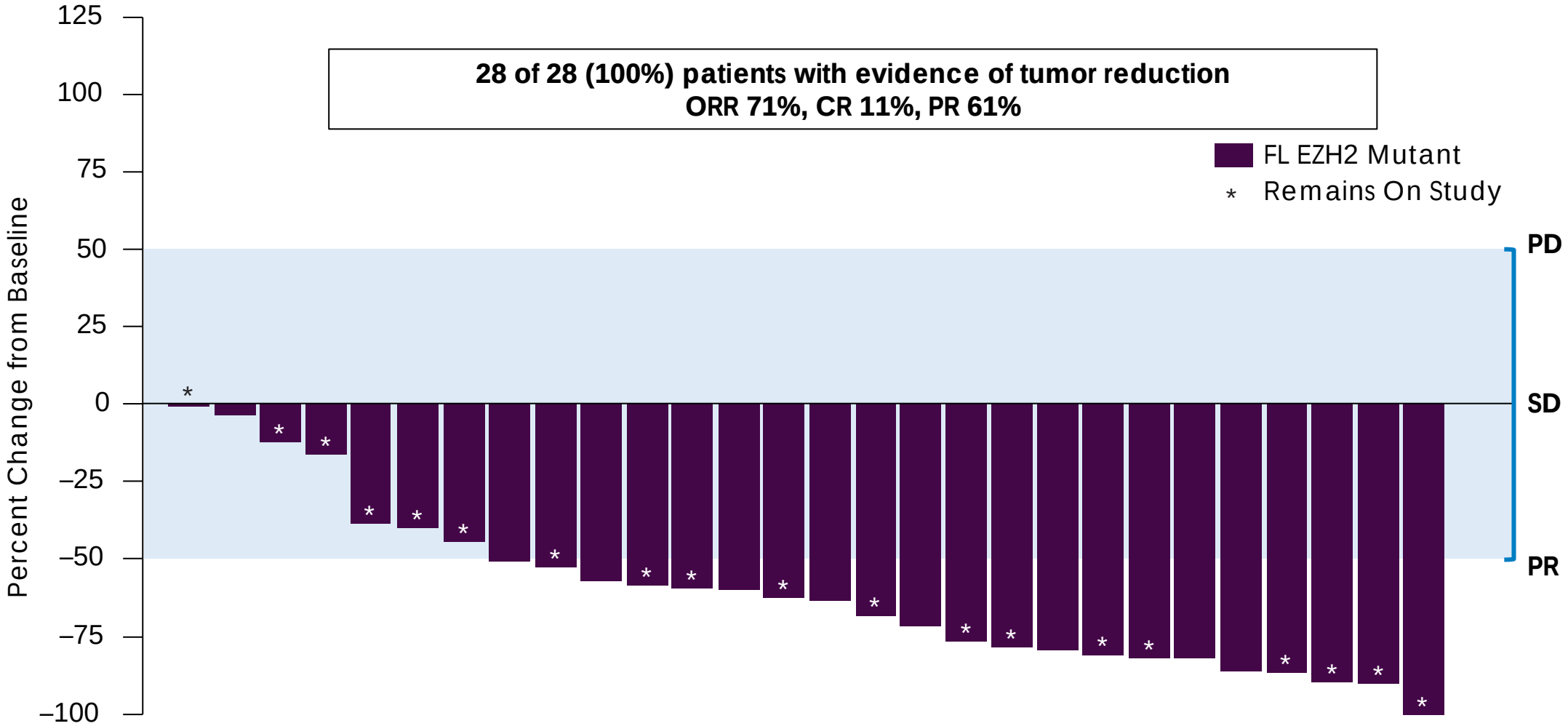
Data as of 01 May 2018. [a] Sum of nodal plus extranodal; [b] Refractory to last regimen defined as SD or PD as best response to most recent prior therapy.

ACTIVITY AND DURABILITY OBSERVED ACROSS BOTH COHORTS

Best Response	FL EZH2 MT (n=28)	FL EZH2 WT (n=54)
Objective response rate (CR + PR), n (%)	**20 (71)**	**18 (33)**
95% CI[1]	51-87%	21-47%
Best response, n(%)		
Complete response (CR)	3 (11)	3 (6)
Partial response (PR)	17 (61)	15 (28)
Stable disease (SD)	8 (29)	17 (31)
Study drug ongoing	6 (21)	1 (2)
Progressive disease (PD)	0	17 (31)
No data/unknown (UNK)	0	2 (4)
Median time to first response[2,3], weeks	11.9	15.9
Median duration of response[2,3], weeks	32.3+	76.0+
Patients with ongoing response[3,4], n (%)	11 (55)	10 (56)
Median progression-free survival[3,4], weeks	48.6+	29.9
Median progression-free survival (responders)[3,4], weeks	48.6+	84.3+

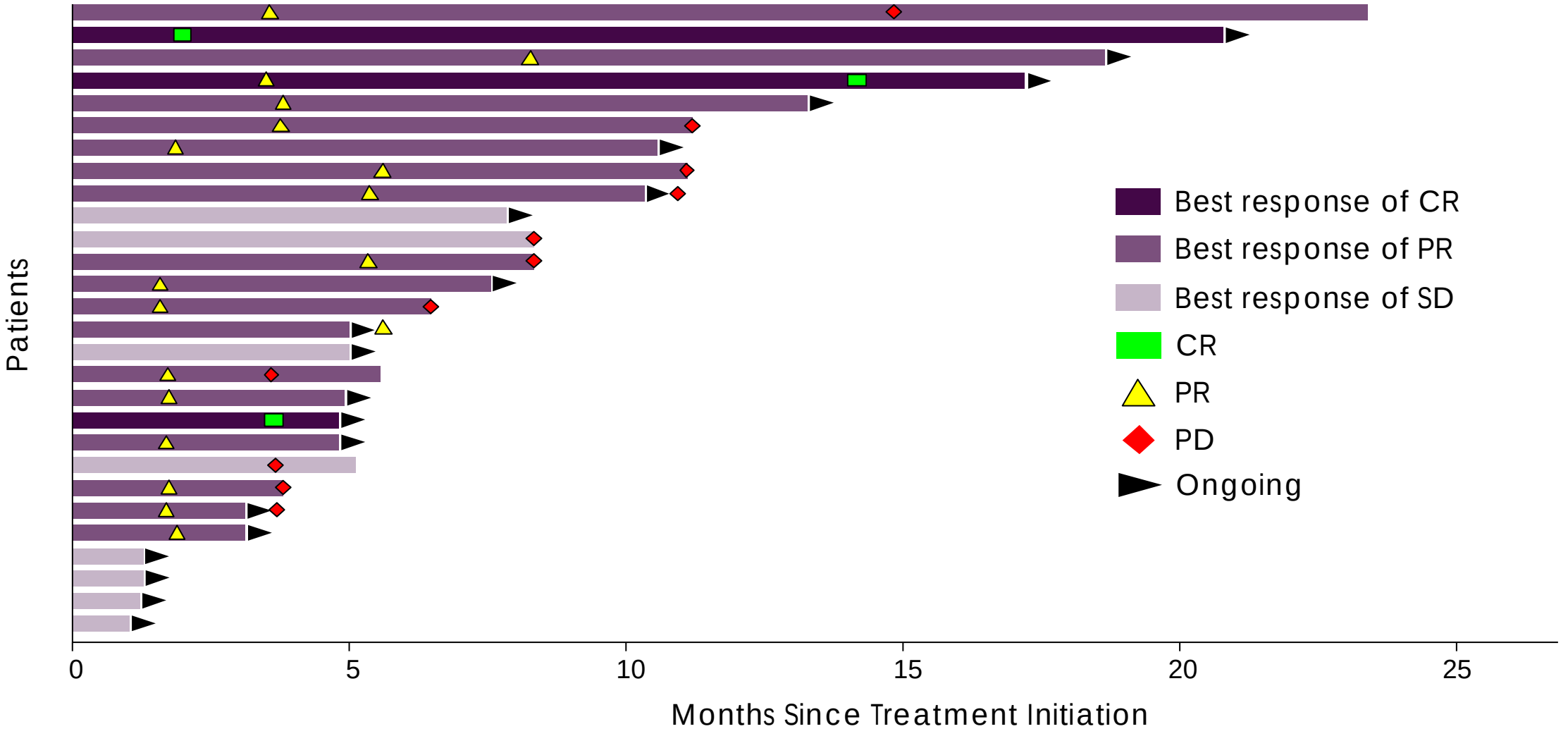
Data as of 01 May 2018. Ongoing patients with best response of 'No Data, Unknown' are not included in this table. Patients that discontinued due to clinical or radiological progression without a valid response assessment are included in PD. [1] By Clopper-Pearson exact confidence interval. [2] Calculated with Kaplan-Meier analysis. [3] Not including time from Rollover study EZH-501. [4] Includes discontinued patients with response ongoing at time of discontinuation. +, Cohort median not yet reached.

TUMOR CHANGE FROM BASELINE FOR MUTATED EZH2 FL PATIENTS



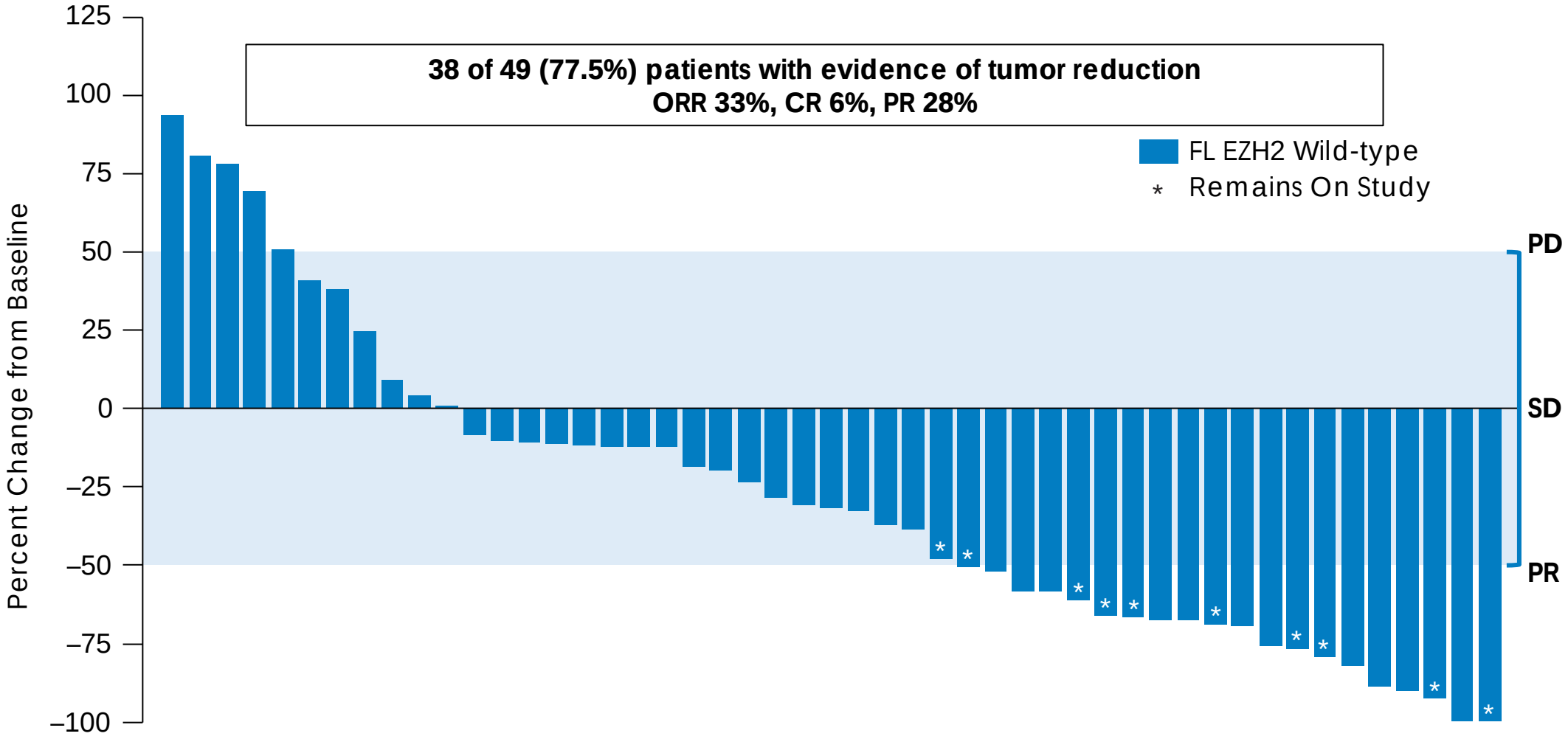
Data as of 01 May 2018. Plot does not include tumor measurements or status from Rollover study EZH-501. Per Cheson 2007, percent change of sum of target nodal lesion SPD and target extranodal lesion SPD.

TUMOR RESPONSE OVER TIME FOR MUTATED EZH2 PATIENTS



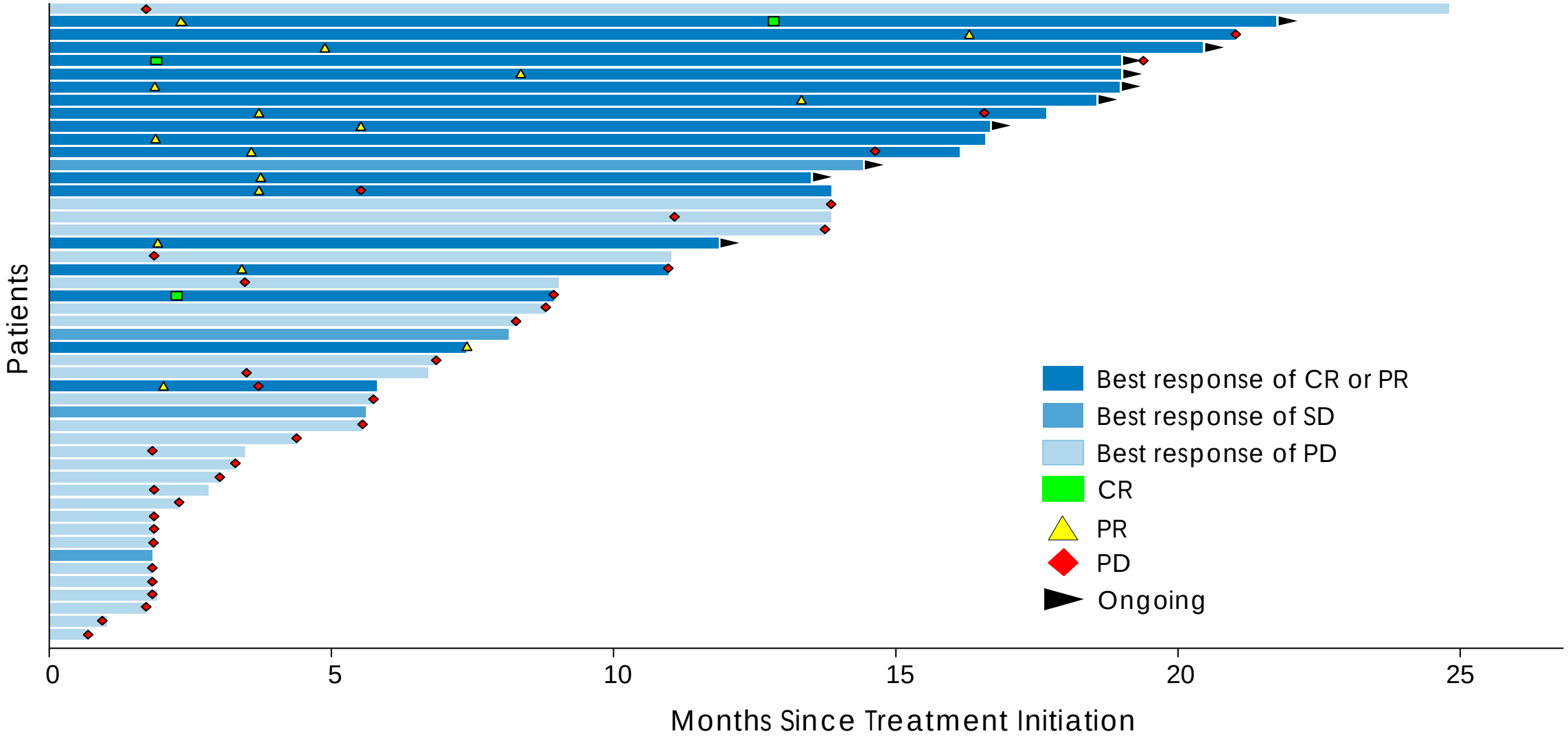
Data as of 01 May 2018. Plot does not include study days from Rollover study EZH-501.

TUMOR CHANGE FROM BASELINE FOR WILD-TYPE EZH2 PATIENTS



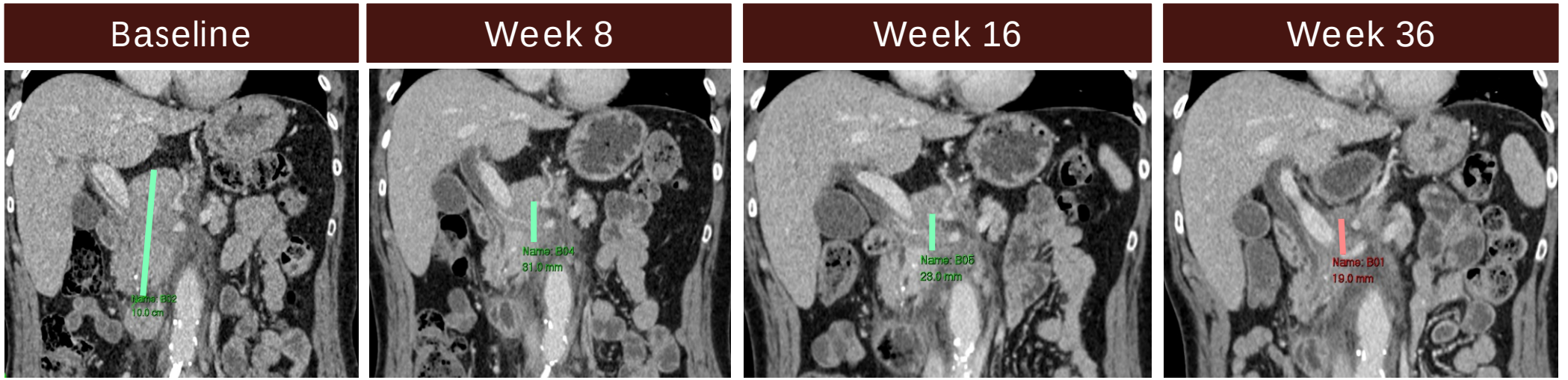
Data as of 01 May 2018. Plot does not include tumor measurements or status from Rollover study EZH-501. Five wild-type FL EZH2 patients are not present as they do not have post-baseline scans. Per Cheson 2007, percent change of sum of target nodal lesion SPD and target extranodal lesion SPD.

TUMOR RESPONSE OVER TIME FOR WILD-TYPE EZH2 PATIENTS

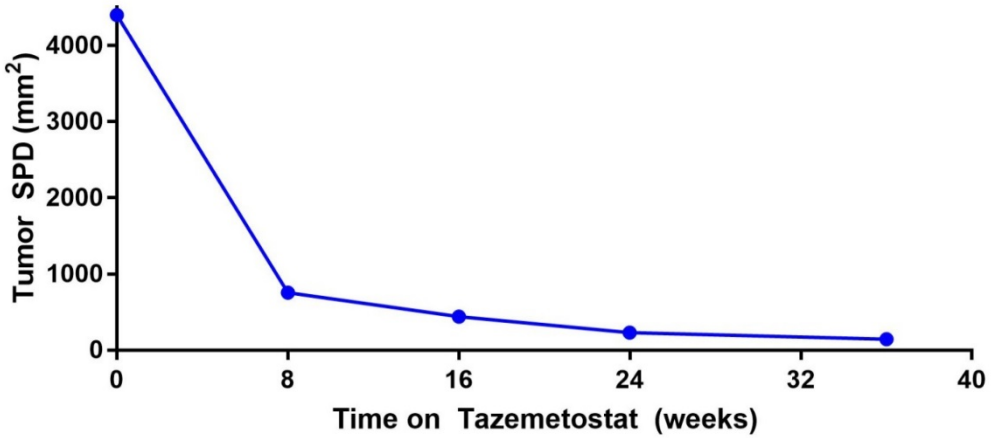


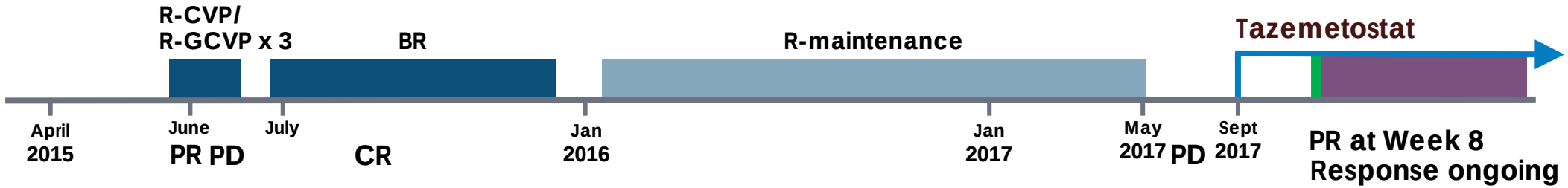
Data as of 01 May 2018. Plot does not include study days from Rollover study EZH-501. Five wild-type FL EZH2 patients are not present as they do not have post-baseline scans.

TUMOR RESPONSE IN A 62 YEAR OLD FEMALE WITH EZH2 MUTATION



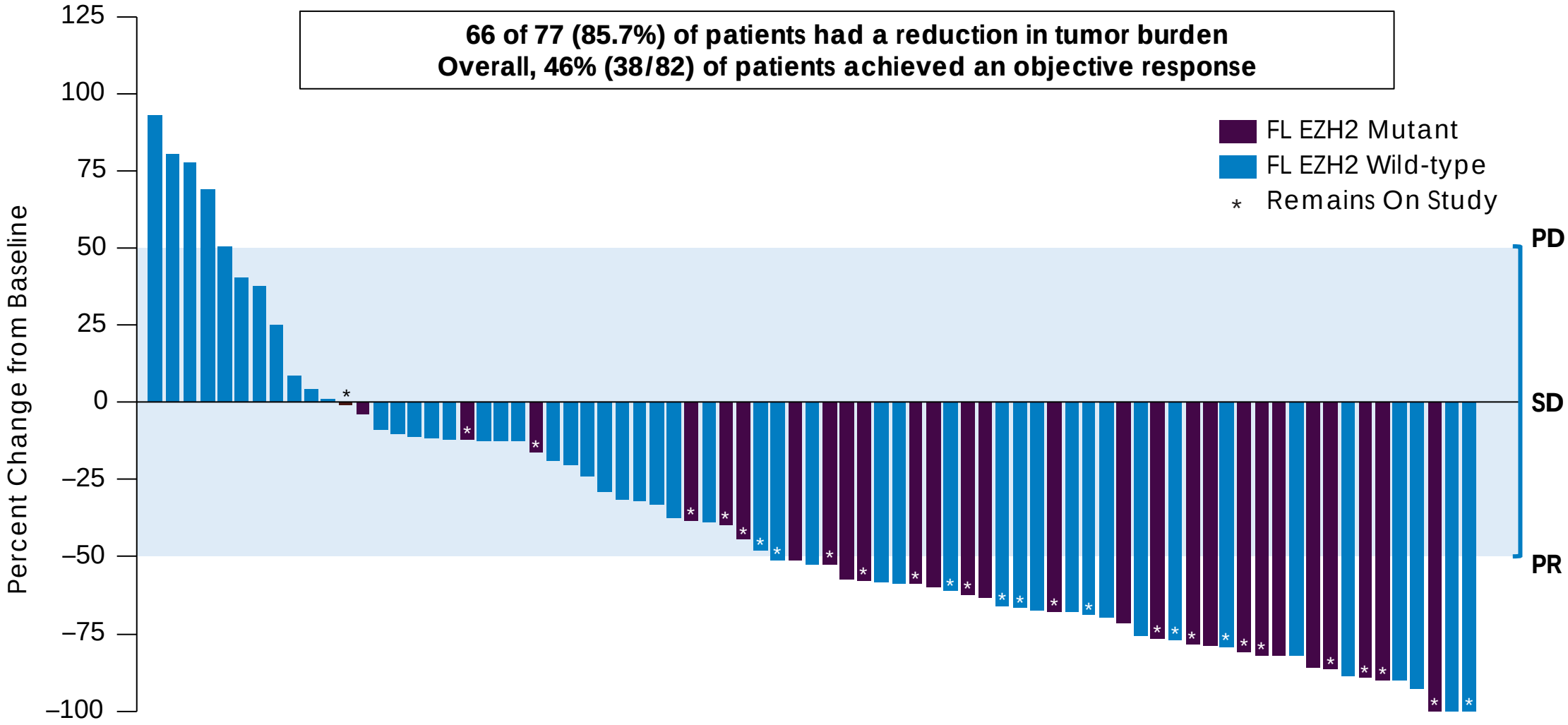
- Diagnosed April 2015
  - G1, Stage II
  - FLIPI score = 4
- 2 prior treatments including R-maintenance





Acknowledgement: Drs. Barwick and Kanfer, Imperial College Healthcare NHS Trust.

TUMOR CHANGE FROM BASELINE FOR FL PATIENTS



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ADVERSE EVENTS LED TO LOW RATE OF DOSE REDUCTIONS AND DISCONTINUATIONS IN FL MONOTHERAPY

Patients, n (%) (N=82)	Treatment-Emergent Adverse Events (TEAEs)[1]	Treatment-related TEAEs
Adverse event (AE), all grades	78 (95)	64 (78)
Grade ≥ 3	33 (40)	14 (17)
Serious AE	20 (24)	3 (4)
AE leading to dose interruption	24 (29)	15 (18)
AE leading to dose reduction	4 (5)	4 (5)
AE leading to drug discontinuation or study withdrawal	9 (11)	5 (6)

[1] All treatment emergent adverse events that first appear during treatment, which were absent before or which worsen relative to the pre-treatment.

FEW TREATMENT-RELATED GRADE ≥3 ADVERSE EVENTS WERE OBSERVED

Adverse Event, n (%)	Patients (N=82)			
	Treatment Emergent Adverse Events (TEAEs)		Treatment-Related TEAEs	
	All Grades	Grade ≥3	All Grades	Grade ≥3
Nausea	18 (22)	1 (1)	16 (20)	0
Fatigue	15 (18)	2 (2)	11 (13)	1 (1)
Anemia	14 (17)	5 (6)	11 (13)	3 (4)
Asthenia	12 (15)	3 (4)	8 (10)	1 (1)
Cough	12 (15)	0	1 (1)	0
Diarrhea	12 (15)	0	9 (11)	0
Upper respiratory tract infection	12 (15)	0	0	0
Alopecia	11 (13)	0	9 (11)	0
Back pain	10 (12)	0	0	0
Bronchitis	10 (12)	0	4 (5)	0
Headache	10 (12)	0	4 (5)	0
Thrombocytopenia	10 (12)	5 (6)	8 (10)	3 (4)
Abdominal pain	9 (11)	1 (1)	2 (2)	0
Muscle spasms	9 (11)	0	5 (6)	0
Pyrexia	9 (11)	0	1 (1)	0
Vomiting	9 (11)	1 (1)	4 (5)	0

Data as of 01 May 2018. Adverse events reported in ≥10% of patients.

SUMMARY

- Interim data from this phase 2 study of tazemetostat demonstrated clinical activity in heavily pretreated patients
  - 71% ORR in patients with mutated EZH2
    - All patients showed a reduction in tumor volume
    - 35 patients (78%) dosed as of June 8, 2018
  - 33% ORR in patients with wild-type EZH2
    - Enrollment is complete
- Durable clinical responses and progression-free survival were observed in patients with or without an activating EZH2 mutation
- Tazemetostat was generally well tolerated
- Promising results from these interim data continue to support EZH2 as a potential novel and valid therapeutic target in relapsed/refractory follicular lymphoma