Fig. 1

First-in-human Phase 1 Trial

- EPZ-6438 (tazemetostat): oral dosing from 100 mg to 1600 mg BID
- Population: relapsed or refractory B-cell lymphoma or solid tumors
- Study design: 3+3 dose-escalation
  - Expansion cohorts at 800 mg (n=6 planned) and 1600 mg (n=6 planned)
  - Food effect sub-study at 400 mg (n=12 planned)
- Primary endpoint: determination of RP2D/MTD
- Secondary endpoints: safety, PK, PD and tumor response (every 8 wks)
- Data cut-off: 8-Jun-2015

Dose (mg BID)	Patients (n=45)	Solid tumors (n=26)	B-cell NHL (n=19)
100*	6	5	1
200	3	1	2
400	3	2	1
800	14	6	8
1600	12	8	4
Food Effect	7	4	3

* 2 formulations

Fig. 2

Patient Tumor Types

Relapsed or refractory NHL		**n=19 ***
Diffuse large B-cell lymphoma (DLBCL)	GCB	4
	non-GCB	6
	undetermined	3
Follicular lymphoma (FL)		5
Marginal zone lymphoma (MZL)		1
Relapsed or refractory solid tumor		**n=26**
INI1-deficient tumor		10
GI malignancy		7
GU malignancy		5
Sarcoma		3
CNS tumor		1

* 14 NHL patients tested to date: 13 WT + 1 mutant by **cobas**® EZH2 Mutation Test
(in development, Roche Molecular Systems, Inc.)

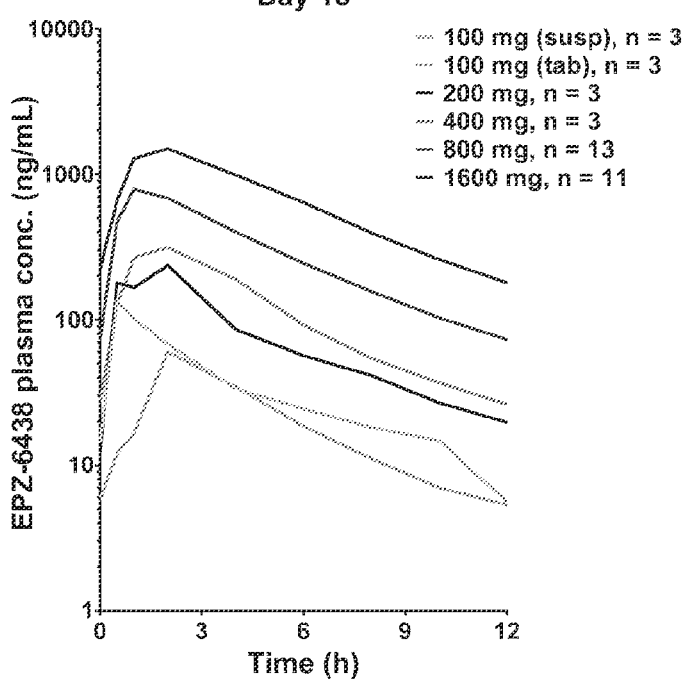
Fig. 3

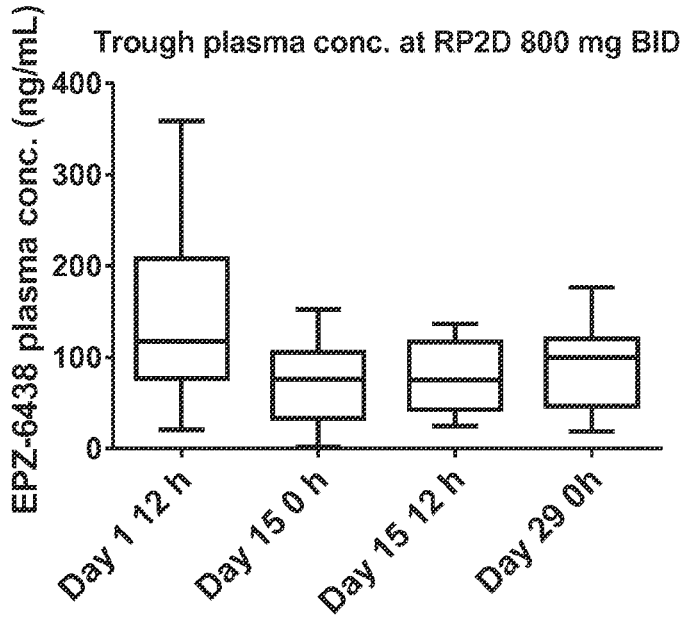
NHL Patient Demographics

Characteristic		Patients (n=19) n (%)
Median age, years (range)		61 (24 - 84)
Sex (M / F)		14 (74) / 5 (26)
# of prior therapeutic regimens	1	2 (10)
	2	1 (5)
	3	7 (37)
	4	2 (10)
	≥5	7 (37)
Refractory to last prior regimen		7 (37)
Prior autologous hematopoietic cell transplant		5 (26)

Fig. 4

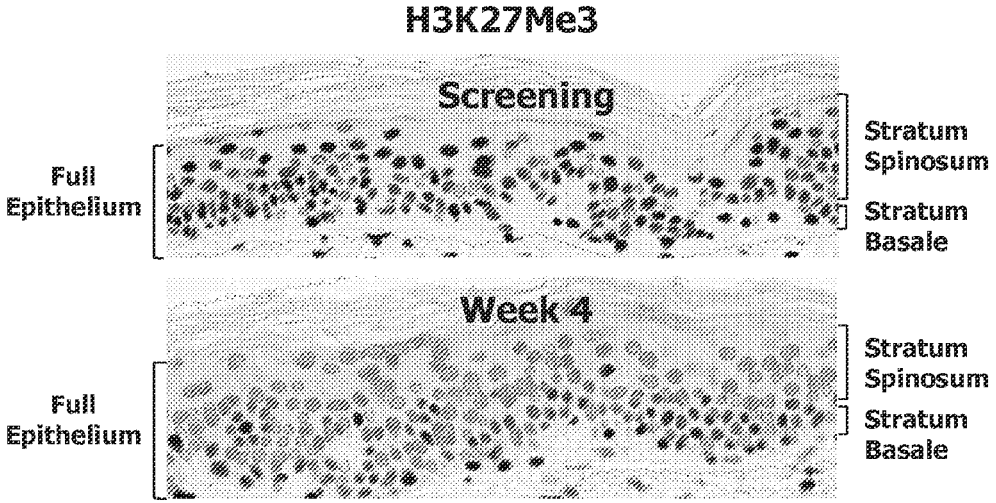
Pharmacokinetics





- Rapid absorption (t_{max} = 1-2 h) with a mean terminal $t_{1/2}$ = 3 - 5 h
- Dose-proportional C_{max} and $AUC_{0\text{-}12h}$ at steady-state (day 15) through 1600 mg BID
- Decrease in systemic exposure between day 1 and day 15 with no further reduction afterwards
  - 42% decrease in $AUC_{0\text{-}12h}$ on day 15 vs. day 1 at 800 mg BID
  - C_{trough} levels reach steady-state by day 15

Fig. 5



Evidence of target inhibition in skin:

- Reduction of H3K27-Me3 IHC signal observed at week 4 at all doses
- Exposure-dependent reductions in H3K27-Me3 IHC signal
- Differential effects by epithelial layer
  - Minimal changes to stratum basale
  - Pronounced changes in stratum spinosum
  - Full epithelium represents composite signal of stratum spinosum and basale

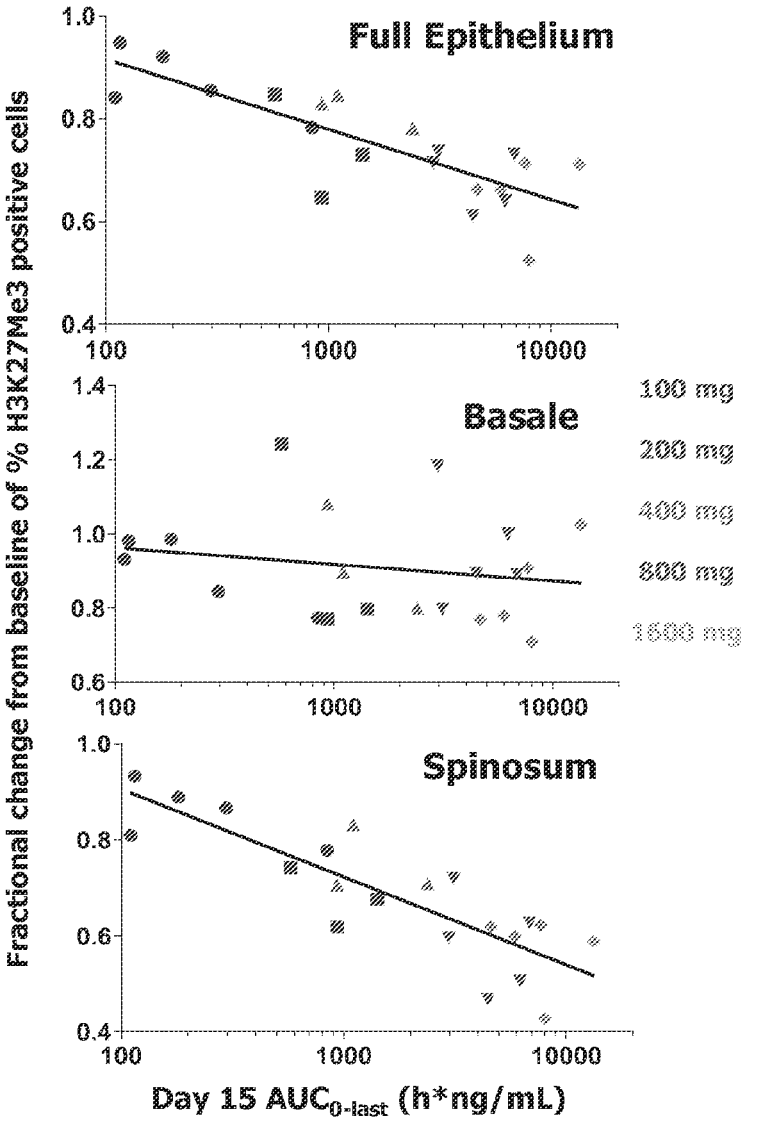


Fig. 6

Patients with:

Dose reduction = 1

Drug discontinuation = 1

Dose interruption = 7

	n = 45			
	All Events		Treatment-Related	
	All Grades *	Grade ≥3	All Grades	Grade ≥3 ‡
Any patient with AE	42	13	29	5
Asthenia	23	1	10	0
Anorexia	11	2	4	1
Anemia	9	1	4	0
Dyspnea	9	0	0	0
Nausea	8	0	6	0
Constipation	7	0	2	0
Vomiting	6	0	3	0
Thrombocytopenia	6	2	4	1
Dyspepsia	5	0	5	0
Muscle spasm	5	0	2	0
Hypertension	4	1	2	1
Neutropenia	2	1	2	1
Transaminase ↑	2	1	1	1

* >10% of patients

‡ all patients

Fig. 7

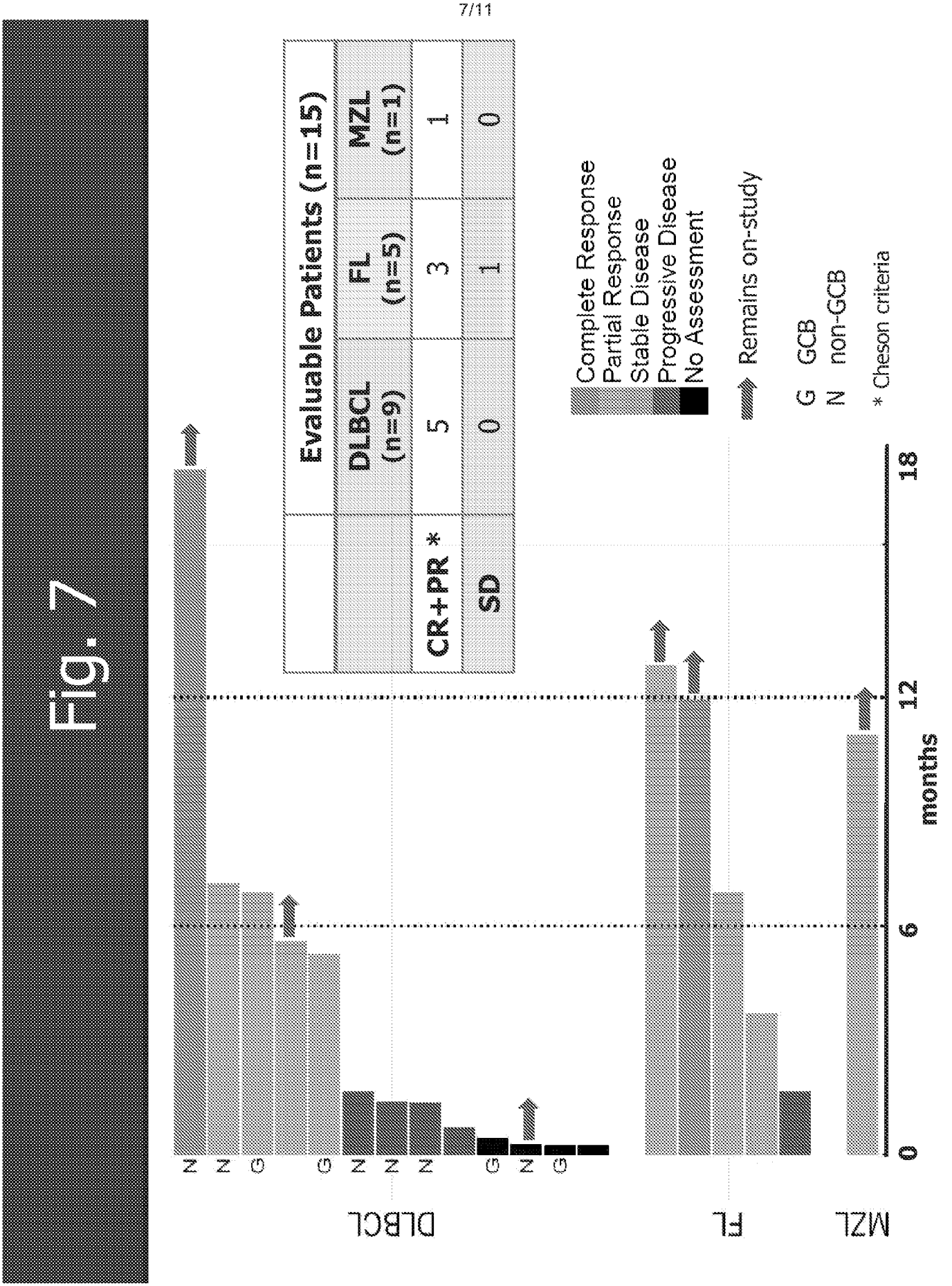

Evaluable Patients (n=15)
DLBCL (n=9)
FL (n=5)
MZL (n=1)
CR+PR *
5
3
1
SD
0
1
0
Complete Response
Partial Response
Stable Disease
Progressive Disease
No Assessment
Remains on-study
G GCB
N non-GCB
* Cheson criteria
DLBCL
FL
MZL
0
6
12
18
months
N N G G N N N G N G

Fig. 8

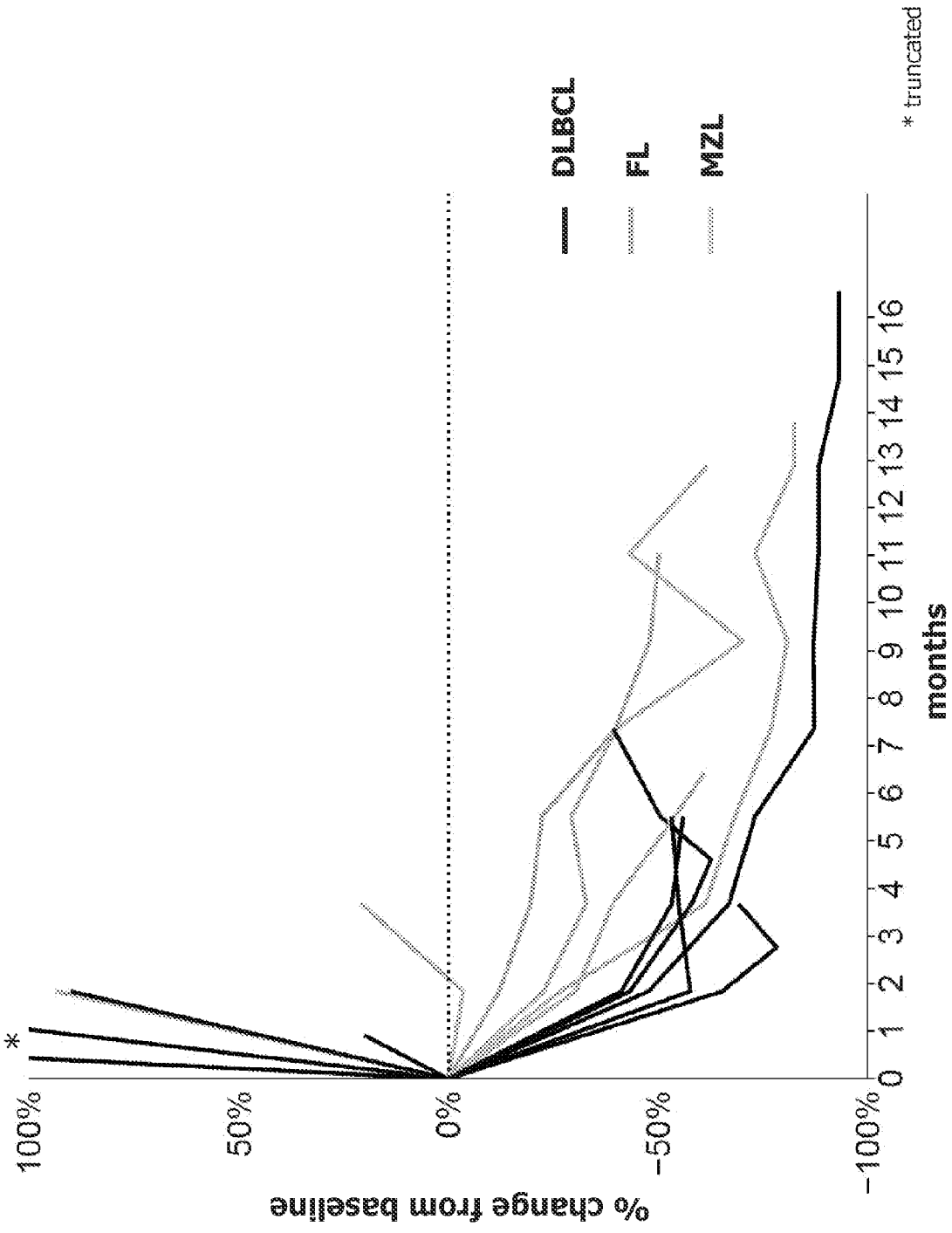

DLBCL
FL
MZL
* truncated
% change from baseline
100%
50%
0%
−50%
−100%
*
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
months

Fig. 9

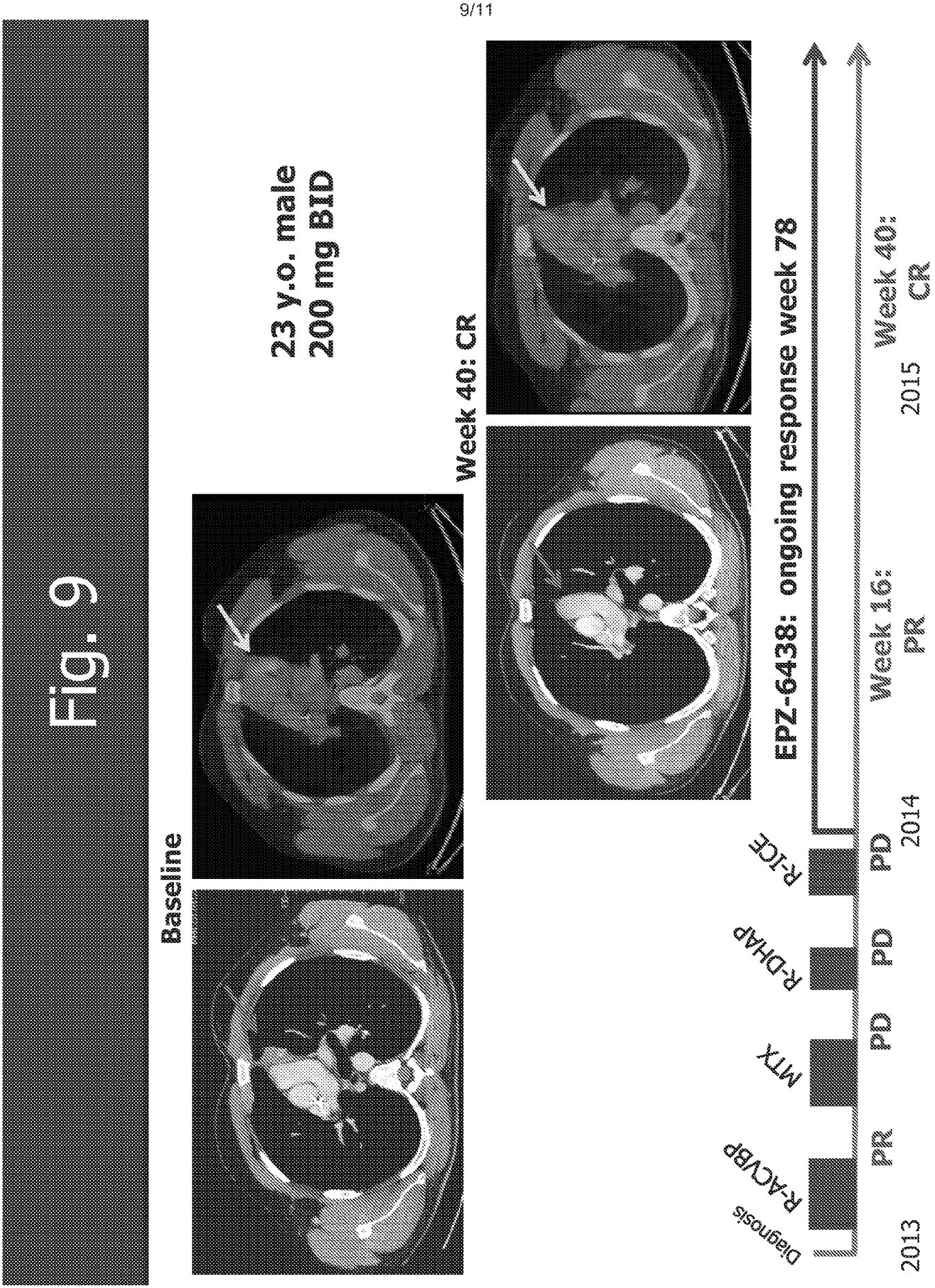

Baseline
23 y.o. male
200 mg BID
Week 40: CR
EPZ-6438: ongoing response week 78
Diagnosis
R-ACVBP
PR
MTX
PD
R-DHAP
PD
R-ICE
PD
2013
2014
Week 16:
PR
2015
Week 40:
CR

Fig. 10

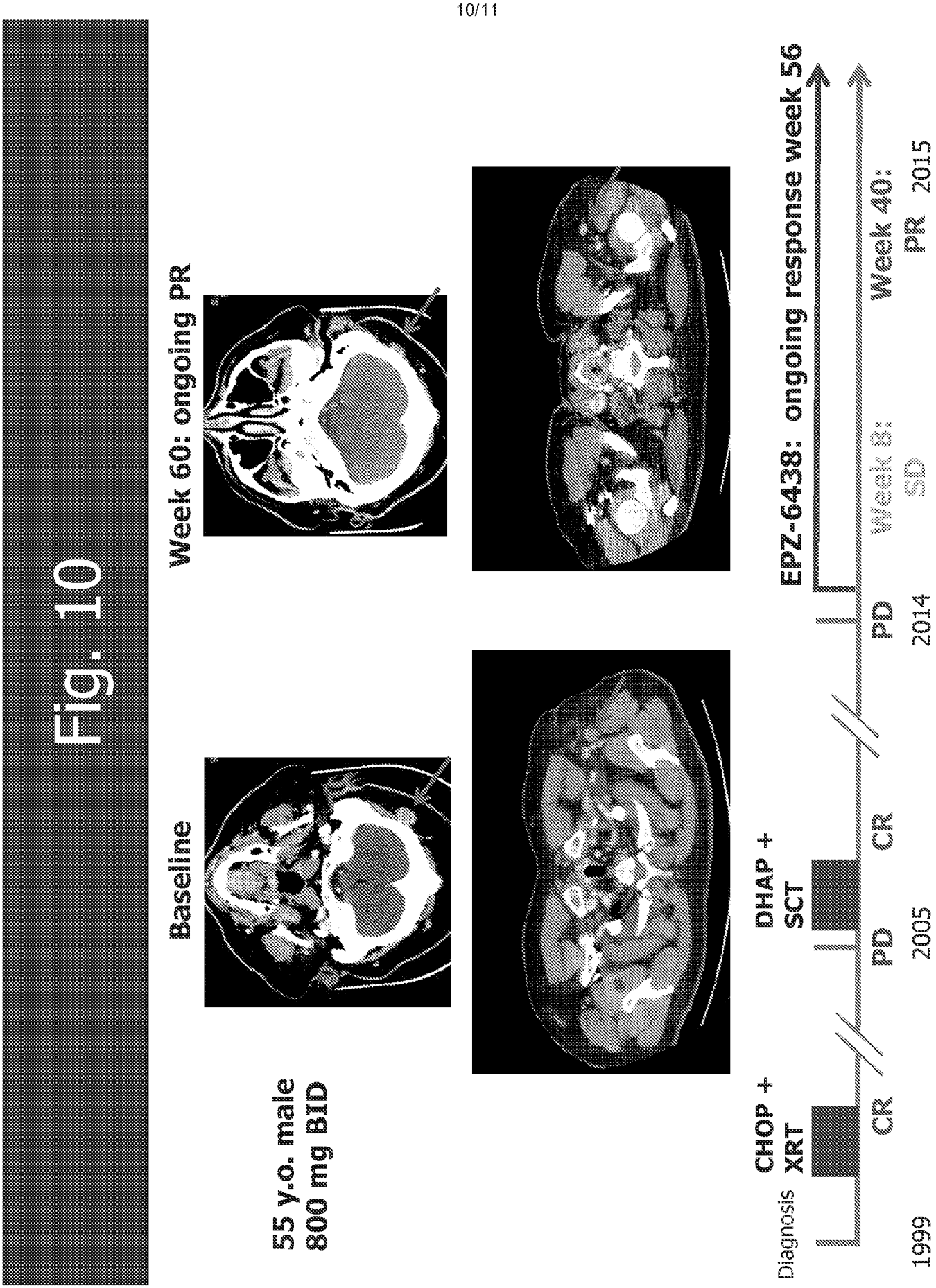
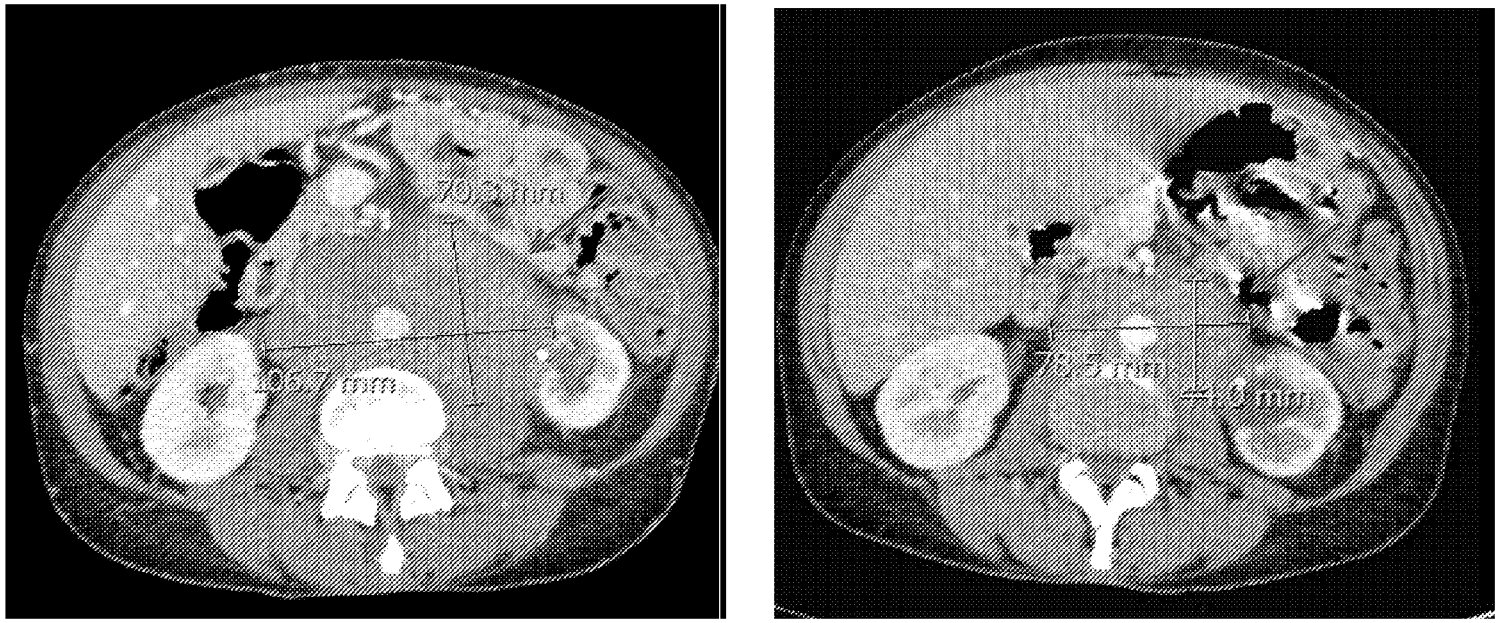

55 y.o. male
800 mg BID
Baseline
Week 60: ongoing PR
Diagnosis
1999
CHOP +
XRT
CR
PD
2005
DHAP +
SCT
CR
PD
2014
EPZ-6438: ongoing response week 56
Week 8:
SD
Week 40:
PR
2015

Fig. 11

Baseline **Week 16: PR**

53 y.o. female
800 mg BID



Mutant by **cobas**® EZH2 Mutation Test (in development). Confirmed Y646H by NGS.

