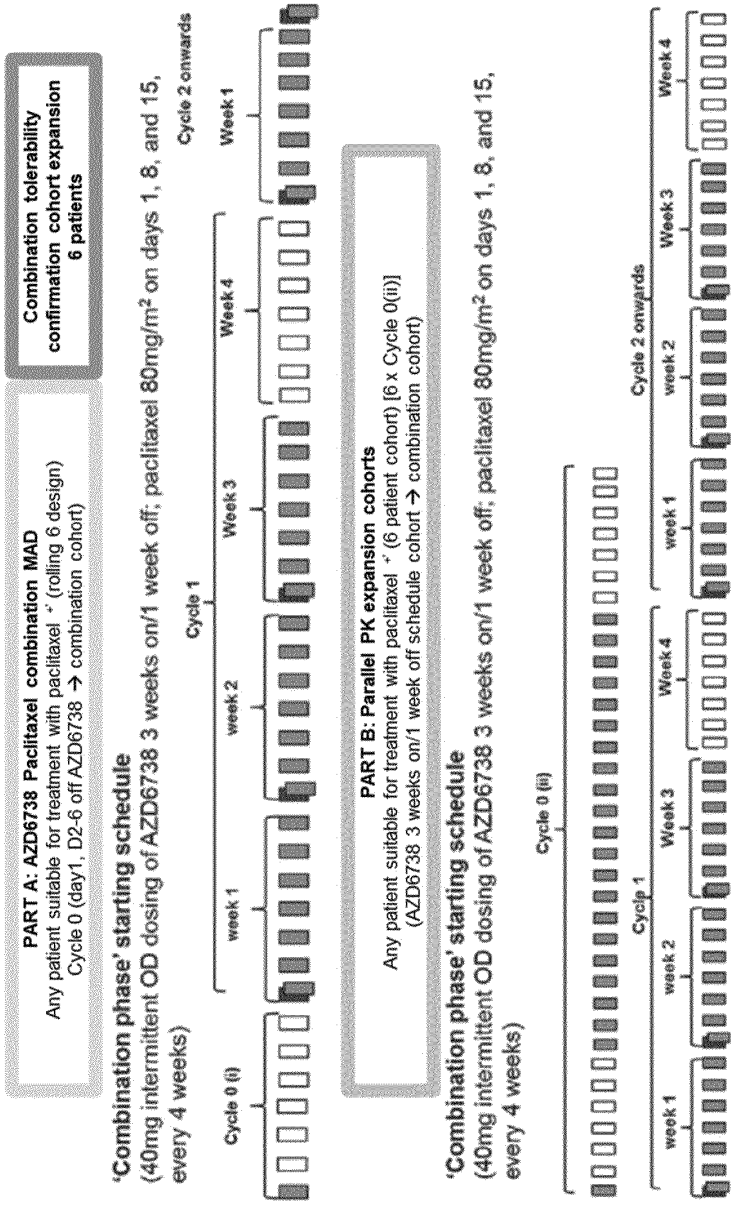

PART A: AZD6738 Paclitaxel combination MAD
Any patient suitable for treatment with paclitaxel +/- (rolling 6 design)
Cycle 0 (day1, D2-6 off AZD6738 → combination cohort)
Combination tolerability confirmation cohort expansion 6 patients
'Combination phase' starting schedule
(40mg intermittent OD dosing of AZD6738 3 weeks on/1 week off; paclitaxel 80mg/m2 on days 1, 8, and 15, every 4 weeks)
Cycle 0 (i)
Cycle 1
week 1
week 2
Week 3
Week 4
Cycle 2 onwards
Week 1
PART B: Parallel PK expansion cohorts
Any patient suitable for treatment with paclitaxel +/- (6 patient cohort) [6 x Cycle 0(ii)]
(AZD6738 3 weeks on/1 week off schedule cohort → combination cohort)
'Combination phase' starting schedule
(40mg intermittent OD dosing of AZD6738 3 weeks on/1 week off; paclitaxel 80mg/m2 on days 1, 8, and 15, every 4 weeks)
Cycle 0 (ii)
Cycle 1
week 1
week 2
Week 3
Week 4
Cycle 2 onwards
week 1
week 2
Week 3
Week 4

Figure 1

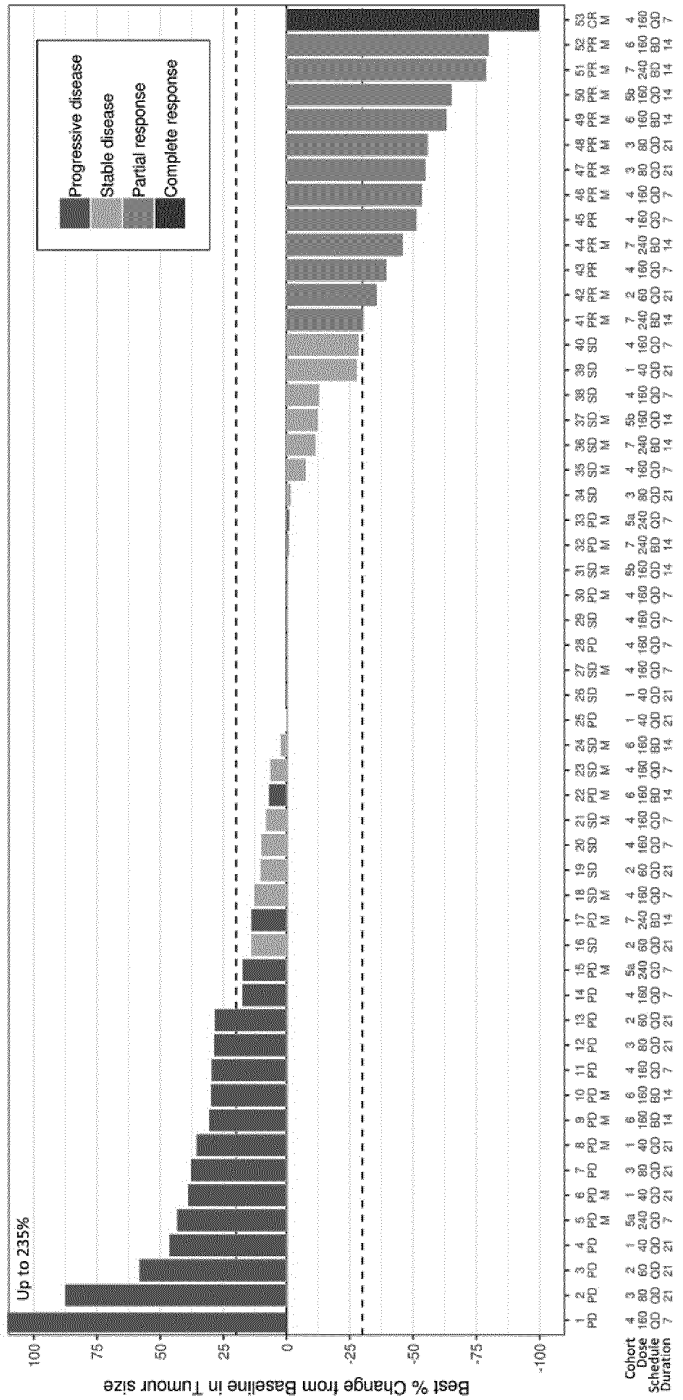

Progressive disease
Stable disease
Partial response
Complete response
Up to 235%
Best % Change from Baseline in Tumour size
100
75
50
25
0
-25
-50
-75
-100
Cohort
Dose
Schedule
Duration

Figure 2

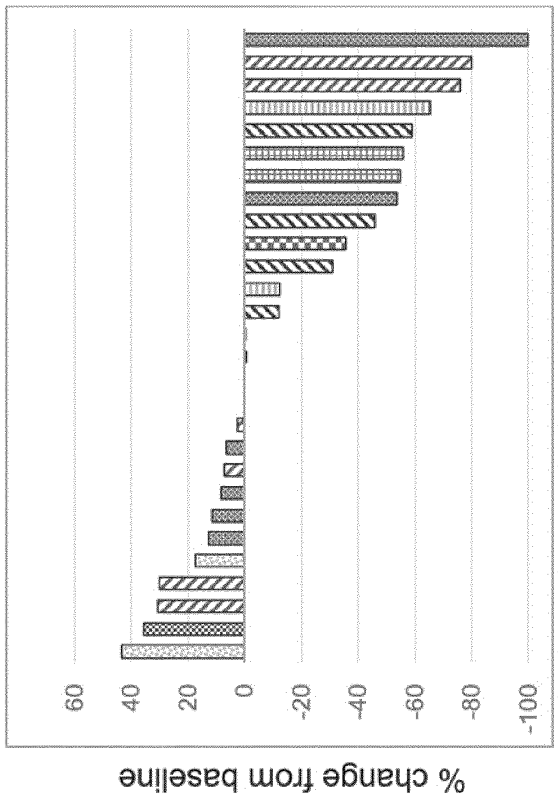

40 mg OD days 1-21
60 mg OD days 1-21
80 mg OD days 1-21
160 mg OD days 1-7
240 mg OD days 1-7
160 mg OD days 1-14
160 mg BD days 1-14
240 mg BD days 1-14
Cohort 5
60
40
20
0
-20
-40
-60
-80
-100
% change from baseline

Figure 3

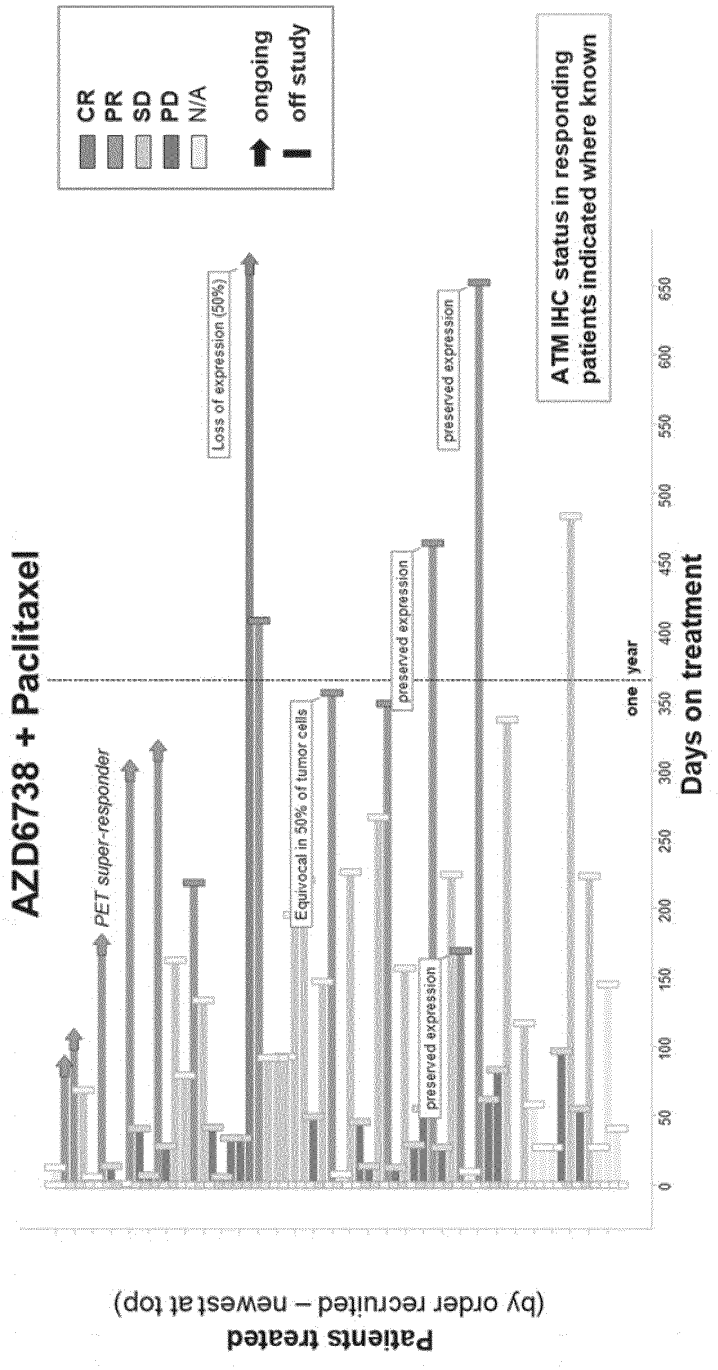

AZD6738 + Paclitaxel
CR
PR
SD
PD
N/A
ongoing
off study
ATM IHC status in responding patients indicated where known
PET super-responder
Loss of expression (50%)
Equivocal in 50% of tumor cells
preserved expression
preserved expression
preserved expression
one year
0
50
100
150
200
250
300
350
400
450
500
550
600
650
Days on treatment
Patients treated
(by order recruited – newest at top)

Figure 4

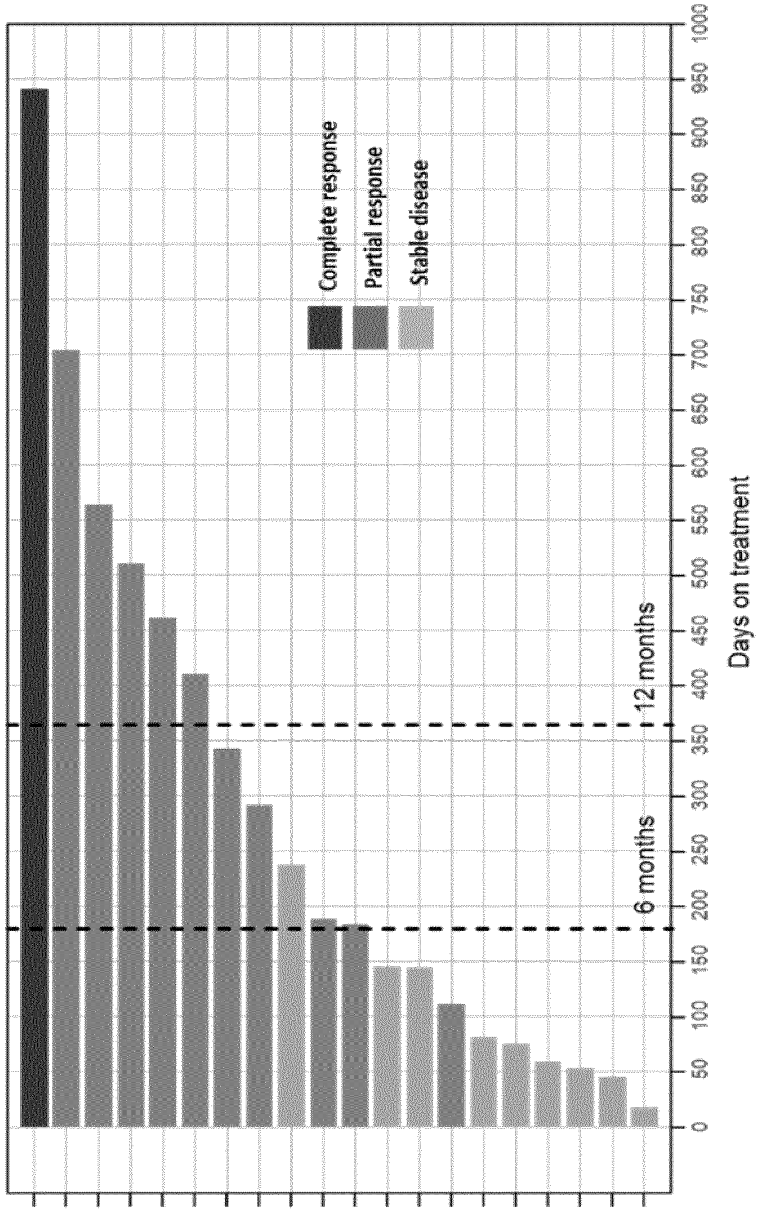

Complete response
Partial response
Stable disease
6 months
12 months
Days on treatment
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900
950
1000

Figure 5