

Clinical Benefit in Biomarker-Positive Patients With Locally Advanced or Metastatic Solid Tumors Treated With the PARP1/2 Inhibitor Pamiparib in Combination With Low-Dose Temozolomide

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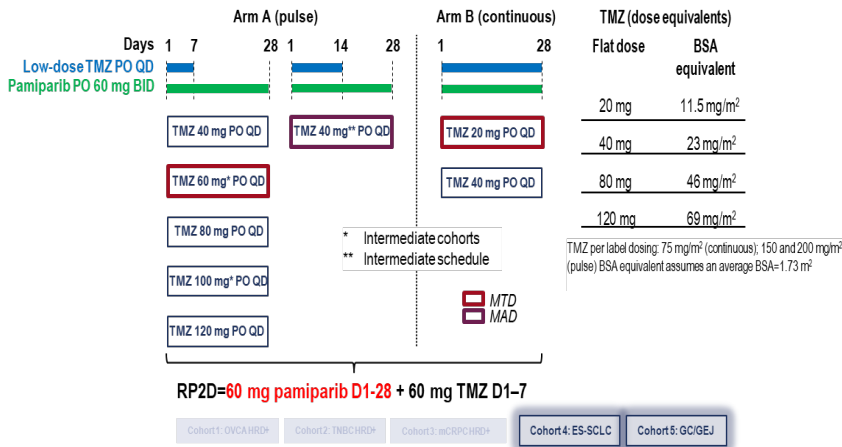


DISCLOSURE INFORMATION

Dr. Calvo reports grants and other from Boehringer-Ingelheim, Roche/Genentech, BMS, Novartis PsiOxus, Nanobiotix Janssen, Abbvie, PharmaMar, PUMA, Sanofi, Lilly, Pfizer, Merck, Nektar, Amcure, Amgen, AstraZeneca, Principia Bayer, CytomX, H3, Incyte, Kura, LOXO, Macrogenics, Menarini, Merck, Serono, Merus, Millenium, Rigontec, Tahio, and Tesaro outside of the submitted work.

Dr. Calvo reports other potential conflicts of interest from Janssen-Cilag, Seattle Genetics, Pierre Fabre, Cerulean Pharma, EUSA, Celgene, START, HM Hospitals Group, Oncoart Associated, International Cancer Consultants, Novartis, Nanobiotix, PsiOxus Therapeutics, Abbvie, AstraZeneca, Guidepoint Global, Roche/Genentech, GLG, Pfizer, Servier, Amcure, BeiGene, and NPO Foundation Intheos (Investigational Therapeutics in Oncological Sciences) all outside the submitted work.

Study Design and Patient Demographics



The study (BGB-290-103, NCT03150810) enrolled a total of 114 patients in dose-escalation and dose-expansion

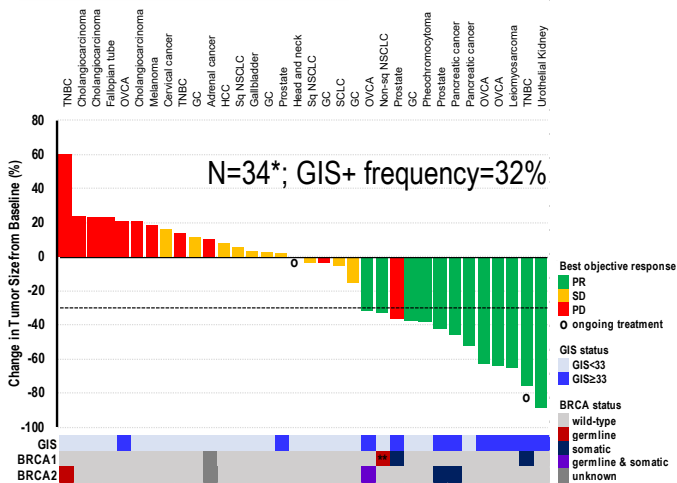
The majority of the patients were white (75%) and were heavily pretreated (median prior therapies of three, range 1-10)

Median study follow-up time of 8.4 months (range 0.3-30.0)

data cutoff date: April 2020

- Samples from dose-escalation and dose-expansion patients were included in the analysis
- Myriad myChoice HRD test performed in archival tissue samples obtained at baseline
 - *Genomic instability score (GIS, formerly HRD score) based on large-scale transitions, telomeric allelic imbalance, and loss of heterozygosity*
 - *GIS+ defined as GIS score ≥ 33*
- ctDNA NGS DNA-Seq performed in blood samples obtained at baseline
 - *Focus on 16 core DNA damage response (DDR) genes:
ATM, ATR, BARD1, BRCA1, BRCA2, BRIP1, CHEK1, CHEK2, CDK12, FANCL, PALB2, PP2R2A, RAD51B, RAD51C, RAD51D, RAD54L*
 - *DDR+ defined as ≥ 1 mutation in one of 16 DDR genes*
- Correlation of DDR/GIS status with overall response rate (ORR) and disease control rate (DCR)

GIS+ Patients Had Better ORR and DCR than GIS- Patients, Irrespective of BRCA Mutation Status



*Patients with postbaseline tumor assessments and Myriad myChoice results.

** The gBRCA1 mutation reported for the nonsquamous NSCLC patient was non-pathogenic.

GIS (formerly HRD score) measures LST+TAI+LOH; GIS+ = GIS score ≥33

ORR

	BRCA1/2mut (N=7)	BRCA1/2wt (N=27)	Total (N=34)
GIS+	100.0% (5/5) (90% CI, 0.55-1.00)	66.7% (4/6) (90% CI, 0.27-0.94)	81.8% (9/11) (90% CI, 0.53-0.97)
GIS-	50.0% (1/2) (90% CI, 0.03-0.97)	9.5% (2/21) (90% CI, 0.02-0.27)	13.0% (3/23) (90% CI, 0.04-0.30)

DCR

	BRCA1/2mut (N=7)	BRCA1/2wt (N=27)	Total (N=34)
GIS+	100.0% (5/5) (90% CI, 0.55-1.00)	83.3% (5/6) (90% CI, 0.42-0.99)	90.9% (10/11) (90% CI, 0.64-1.00)
GIS-	50.0% (1/2) (90% CI, 0.03-0.97)	57.1% (12/21) (90% CI, 0.37-0.75)	56.5% (13/23) (90% CI, 0.38-0.74)

- In this limited subset of patients treated with pamiparib in combination with different doses of LD TMZ, GIS+ patients derived superior benefit, irrespective of *BRCA1/2* mutation status, compared with DDR+, GIS-, and DDR- patients
- Responses in the DDR+ subpopulation were primarily associated with *BRCA1/2* mutations
- GIS status, which is a global measure of genomic instability, appears to be a robust biomarker to predict response to pamiparib + LD TMZ
- As previously shown, mutations in DDR genes other than *BRCA1/2* have limited utility in predicting the response to PARP inhibitors
- A new cohort, cohort 6, is currently evaluating the antitumor activity of pamiparib + LD TMZ in patients with GIS+ NSCLC, head and neck, esophageal, and soft tissue sarcoma tumors

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