

#25P: DIFFERENTIAL RESPONSE TO PLATINUM AGENTS OF PATIENTS CARRYING THE GERMLINE BRCA1 c.211 A>G PATHOGENIC VARIANT

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BACKGROUND

The presence of somatic and/or germinal mutations in the genes **BRCA1** and **BRCA2** is known to be **predictive of response to platinum** agents and inhibitors of PARP (iPARP) in ovarian cancer. Recently, it has been shown that the efficacy can vary according to the specific mutation^{1,2}.

In our community there is a high prevalence of patients (pts) carrying the **BRCA1 c.211 A>G germline pathogenic variant**, which is a founder mutation originated in the northwest of Spain.

The aim of our study was to evaluate if these pts presented **different outcomes** when treated with first line platinum agents.

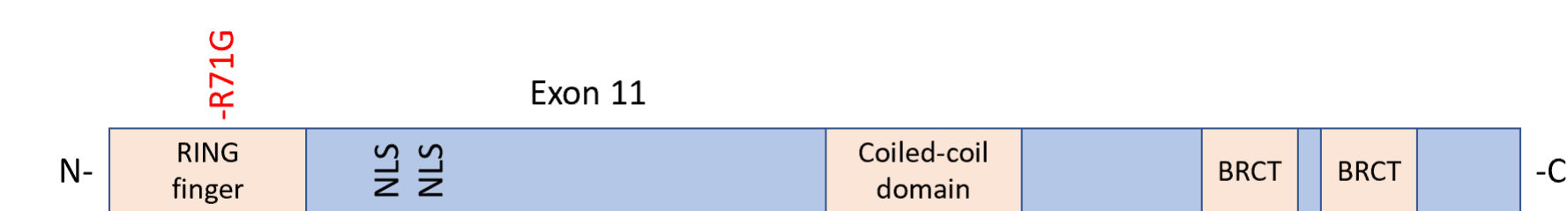


Figure 1. BRCA1 structure and localization of the R71G pathogenic variant

METHODS

We performed a **single-centre retrospective** analysis of pts carrying somatic and/or germline pathogenic variants of **BRCA1** and **BRCA2** treated with platinum agents and iPARP between January 2014 and December 2021.

Variants were detected with validated methods in tissue and/or blood samples. Data was extracted from electronic health records and analysed with SPSS software

RESULTS

Baseline Patient Characteristics (n = 38)	
Age yr (Me, range)	56.4 (40 - 82)
FIGO Stage no. (%)	
IIIC	22 (57.9)
IV	13 (34.2)
BRCA 1 pathogenic variant no. (%)	25 (65.8)
BRCA 1 c.211 A>G variant no. (%)	12 (31.6)

Patients with the BRCA1 c.211 A>G variant presented a **worse objective response rate (ORR)** to first line platinum-based chemotherapy when compared to all the pts (**58.3% vs 88.5%, p = 0.03**) and to BRCA1 mutated pts (58.3% vs 84.6%, p = 0.14).

Median progression free survival (PFS) to first line treatment was not *significantly* different among BRCA1 c.211 A>G variant carriers and the rest of the pts (21 vs 27 months, p= 0.44), and neither was overall survival (OS) (72 vs 91 m, p = 0.27).

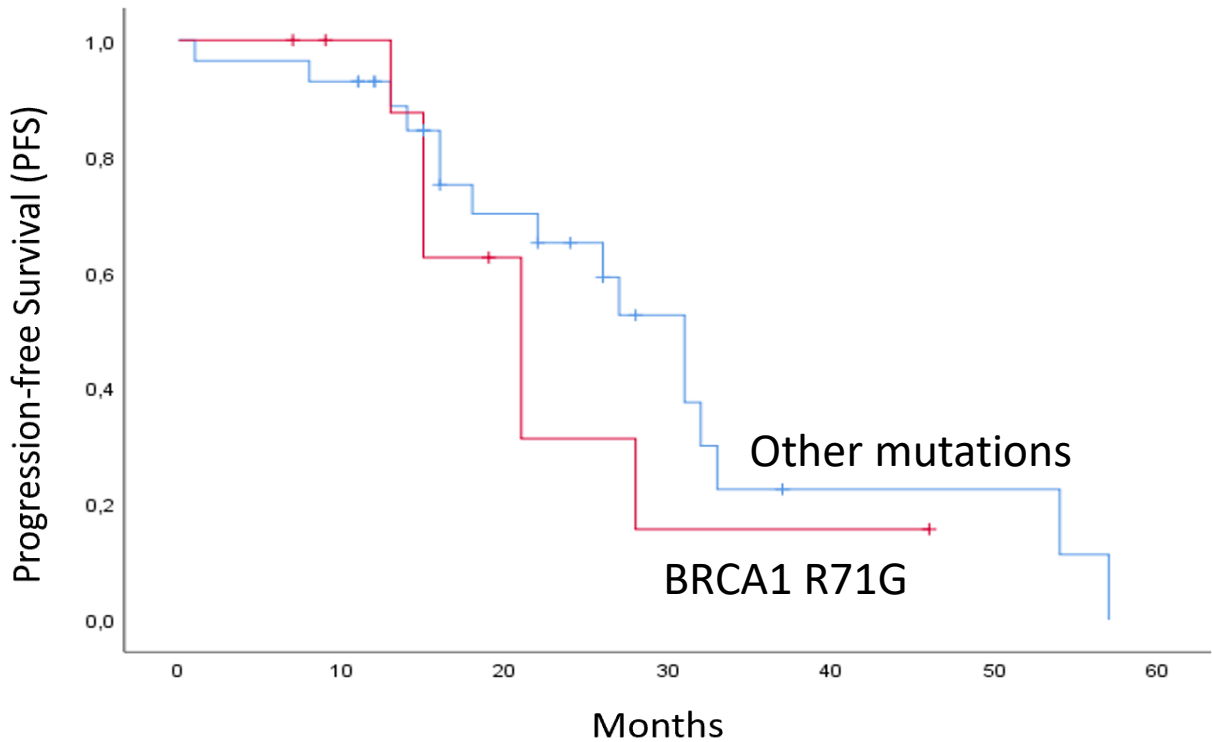


Figure 2. PFS of pts with BRCA1 R71G mut vs rest of the population

CONCLUSIONS

Pts with **BRCA1 c.211 A>G germline pathogenic variant** treated in our centre had a **worse response rate to platinum-based chemotherapy** even though PFS and OS were not significantly different. Further research should be carried out to test if this mutation conveys **less sensitivity to DNA damaging agents**

REFERENCES

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