### INTRODUCTION

Tumour mutational burden (TMB) has been shown to be a predictor of checkpoint inhibitor response. However, up to 25% of patients with mCRPC harbour a deleterious germline or somatic alteration in BRCA1, BRCA2, ATM or other homologous recombination repair (HRR) genes, and may benefit from treatment with a PARP inhibitor as a single agent.

The phase 2 TRITON2 (NCT02952534) and phase 3 TRITON3 (NCT02775344) studies are investigating in-patient samples in patients with mCRPC harboring an alteration in an HRR gene.

### METHODS

A total of 1311 tumour and 638 plasma specimens were collected from 1516 patients to determine patient eligibility for TRITON2 and TRITON3. TRITON3 eligibility is defined by a or 12 other HRR genes (BARD1, BARD2, BWR1, CDK12, CZC1, FANCI, FANCJ, MRE11, NBN, PALB2, RAD51, RAD52, RAD10, RAD14).

Deletions include exome deletions, nonsense mutations, deleterious truncating mutations, protein truncating rearrangements, and (for tissue samples) homozygous loss of function (LOF).

Call-free circulating tumour DNA (ctDNA) from plasma samples was sequenced by Foundation Medicine, Inc. (FMI), using a next-generation sequencing (NGS) assay to identify deleterious germline or somatic alterations in BRCA1, BRCA2, ATM, or 3 additional HRR genes (CDK12, CHEK2, PALB2).

Archival and contemporaneous tissue samples were sequenced by FMI to identify deleterious germline or somatic alterations in BRCA1, BRCA2, ATM, or 12 other HRR genes (BARD1, BARD2, BWR1, CDK12, CZC1, FANCI, FANCJ, MRE11, NBN, PALB2, RAD51, RAD52, RAD10, RAD14).

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### Tissue Tumour Mutational Burden

Tissue tumour mutational burden (TMB) has been shown to be a predictor of checkpoint inhibitor response. However, up to 25% of patients with mCRPC harbour a deleterious germline or somatic alteration in BRCA1, BRCA2, ATM or other homologous recombination repair (HRR) genes, and may benefit from treatment with a PARP inhibitor as a single agent.

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