Precision Choice at the Point of Care

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Abstract

Background and rationale: The most promising treatment advance for ovarian cancer patients in recent years are the poly (ADP-ribose) polymerase inhibitors (PARPi's). These are drugs that help prolong remission time and currently, there is an 'all-comers' approval for their use. There is evidence to support molecular tumor testing in order to quantify the benefit from PARP inhibition, as all patients do not respond equally to treatment. Prolonged remission time ranges from as low as 3 months to as high as 42 months, depending on molecular tumor characteristics. Because PARPi-related toxicities can decrease quality of life for up to 3 months, precision estimates of benefit are needed to promote informed patient decision making.

Objectives: The objectives of this study are to perform tumor testing, provide patients with precision estimates of benefit from PARP inhibition and measure the impact of this information at the point of care. We are also assessing quality of life and duration of benefit of PARPi's in a real-world setting. A cost effectiveness analysis will be completed.

Methods and Results: This is a prospective, non-randomized pragmatic clinical trial that enrolls all women with ovarian cancer who agree to tumor testing and qualify for a PARPi. Tumor testing is completed, which categorizes patients as either 1) BRCA mutant, 2) homologous recombinant deficient but BRCA wild type (HRD) or 3) homologous recombinant proficient (HRP). Patients are then provided with specific estimates about the amount of benefit from taking PARPi therapy. Patients with a BRCA mutation are informed that their prolonged remission time (also called progression free survival - PFS) benefit is 42 months, the HRD positive (BRCA wt) group are informed their benefit is 9 months and the HRD negative (HRP) patients are told their benefit is 3 months. PARPI'S do not extend life. As the benefit is about equal to the risks *for the HRP patients only*, we provide a patient decision aid to help them decide whether a PARPi is right for them. PARPi therapy is recommended for BRCA mutant patients and the HRD patients due to the significant benefit. This trial was activated in September 2023 in Saskatchewan and recently Halifax activated this trial. Fifteen patients are enrolled; 10 are HRP and 60% of these HRP patients (n=6) have decided against a PARPi. All other patients decided to take a PARPi as recommended by their physician.

Conclusion: Preliminary findings confirm that if patients are given precision care and a patient decision aid to help them understand benefits versus risks of therapy, that they will make treatment choices reflective of their own priorities, values and preferences.

Anticipated Impact: The results of this trial will be used to convince provincial governments to make tumor testing in ovarian cancer a funded standard of care.

Plain language summary

TFRI has helped made it possible for us to open a prospective pragmatic trial; the first of its kind in ovarian cancer in Canada. This trial aims to tailor treatment decisions and set a new standard of care in ovarian cancer. We are exploring patient preferences for a precision oncology approach to their care through molecular tumor sequencing and testing. Patients are empowered through promotion and advancement of informed patient decision making, made possible by tumor testing information and a custom patient decision aid. The result is patient control over treatment decisions that affect their quality of life and provision of personalized, reliable and effective treatment options. For the first time, we will also prospectively collect real world evidence regarding the effectiveness and side effects associated with a relatively new class of drugs used to prolong remission time.