INCORPORATING PARP INHIBITION IN CANCER THERAPY: KEY QUESTIONS, EXPERT ANSWERS

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MEETING SUMMARY

This engaging symposium focussed on the rationale and current evidence supporting the role for poly(adenosine diphosphate-ribose) polymerase (PARP) inhibition in patients with cancer. The meeting opened with an overview of DNA repair and the biological basis for targeting this process in oncology, delivered by Prof Calvert. This was followed by a discussion from Prof Pujade-Lauraine that focussed on patient selection for PARP inhibition and the role for these agents in *BRCA*-mutated and *BRCA*-like cancers. Next, Prof Colombo presented a clinical scenario of *BRCA*-associated ovarian cancer and examined optimal treatment options in the first-line setting and for progressive disease. She also highlighted current clinical data and ongoing trials evaluating PARP inhibition in advanced ovarian cancer. Prof Tutt then discussed the potential role for PARP inhibitors in patients with breast cancer, focussing on a clinical scenario of triple-negative disease and emphasising current and investigational treatment options. Lastly, Prof Van Cutsem described emerging data and ongoing clinical studies evaluating PARP inhibition in the treatment of patients with pancreatic and gastric cancers, and how this could impact future clinical practice. The programme also included a PARP quiz, in which participants were polled at the beginning and conclusion of the symposium to examine their knowledge and practice patterns regarding the use of PARP inhibitors in oncology. The key highlights from these presentations and the PARP quiz are summarised herein.

Why Target DNA Repair Mechanisms in Cancer?

Professor Hilary Calvert

Prof Calvert began by discussing the importance of DNA repair in maintaining genomic integrity. Cells endure approximately 10,000–30,000 episodes of DNA damage on a daily basis as a result of replication errors, environmental factors, and other causes.[1] This threat is met with five distinct repair pathways: recombinational repair (homologous recombination and non-homologous end joining [NHEJ]), nucleotide excision repair, mismatch repair, base excision repair (BER), and direct reversal. There is considerable redundancy within the DNA repair system, such that a defect in one pathway can be overcome by the action of a different pathway, and loss or mutation of one repair protein allele can often be compensated for by normal expression of the other allele.

DNA damage repair has important implications in patients with cancer, including mutations in *BRCA1* and *BRCA2*.[2] *BRCA* mutation carriers with one dysfunctional gene can still perform homologous recombination due to the remaining normal gene. However, if DNA damage leads to loss of that remaining *BRCA* gene (a 'second hit'), cells cannot perform homologous recombination repair and are forced to undertake the more error-prone NHEJ instead. This results in accumulation of additional mutations and increased susceptibility to tumour formation.

Prof Calvert described how this deficiency in DNA repair also creates the possibility of synthetic lethal interactions with drugs that inhibit alternative DNA repair pathways.[2] Synthetic lethality results when inhibition of two pathways leads to cell death, while the loss of either pathway alone does not affect viability. Synthetic lethality has been elegantly illustrated by the inhibition of poly(adenosine diphosphate-ribose) polymerase (PARP) in cell lines and tumours with aberrant DNA repair mechanisms. Two articles published in *Nature* showed that cells deficient in *BRCA1/2* were highly sensitive to PARP inhibition and exhibited early cell death.[3,4] In normal cells, PARP activity repairs single-strand breaks via BER. If a PARP inhibitor (PARPi) is present, the break will not be repaired and will lead to double-strand breaks during DNA replication. In cells with one or two functional *BRCA* genes, these double-strand breaks will be repaired by homologous recombination. However, homologous recombination cannot occur in *BRCA*-deficient cells, leading to collapse of the replication fork and cell death. Therefore, the synthetic lethal interaction elicited by PARPi in *BRCA*-mutated cancers is targeted to the tumour cells specifically.

Prof Calvert emphasised that ongoing clinical trials are investigating PARPi alone and in combination regimens in cancers with *BRCA* mutations or deficiency in homologous recombination.[2] The complex role of DNA repair in oncogenesis suggests that additional synthetic lethal interactions may be found with continued investigation.

How to Identify Patients Who May Benefit From PARP Inhibitors

Professor Eric Pujade-Lauraine

Prof Pujade-Lauraine first asked participants to identify the greatest challenge they faced when ordering a *BRCA* test for a patient with advanced ovarian cancer. The responses were evenly divided between *BRCA* testing not being included in their country's national guidelines, *BRCA* testing being restricted to subsets of ovarian cancer according to family history and/or young age, mandatory pre-test genetic counselling delaying results, and non-reimbursement of *BRCA* testing. Prof Pujade-Lauraine agreed that there are substantial hurdles to *BRCA* testing, but emphasised that the time has come for incorporation of genetics into gynaecological oncology.

BRCA testing benefits both patients and their families by providing information on prognosis, treatment decisions, and follow-up. A pooled analysis of 26 observational studies of ovarian cancer showed that *BRCA1/2* carriers had significantly higher 5-year survival rates compared with non-carriers.[5] This improvement in survival may be linked to increased sensitivity to platinum agents and PARPi, informing treatment decisions.[1,6] For families, *BRCA* testing provides risk assessment and the opportunity for prophylactic surgery to reduce cancer risk.

Prof Pujade-Lauraine then discussed which patients with ovarian cancer should be considered for *BRCA* testing. Several population-based studies indicate that younger age and family history are not good predictors of *BRCA* mutation, with a similar median age at diagnosis for *BRCA1/2* mutation

carriers and non-carriers and approximately one-third of *BRCA1/2* mutation carriers having no family history of ovarian or breast cancer.[7-10] Population-based studies also demonstrated that histological type is not a foolproof predictor of *BRCA* status, with *BRCA* mutations detected in tumours of serous, endometrioid, and clear cell histology.[8,9,11]

Current guidelines recommend *BRCA* mutation testing in all patients with epithelial ovarian cancer, regardless of age or family history.[12,13] The current process for *BRCA* testing involves referral for genetic counselling and assessment of germline *BRCA* mutations. However, several studies suggest that an additional 5–7% of patients with ovarian cancer have somatic *BRCA* mutations within the tumour without germline mutations.[14-16] While these somatic mutations do not have implications for the patient's family, they can greatly impact treatment decisions, suggesting that tumour testing should also be considered.

Ongoing efforts are focussed on validating methods to achieve accurate *BRCA* testing results. The emergence of next-generation sequencing (NGS) also creates the opportunity to detect mutations in other genes beyond *BRCA1/2* that block homologous recombination function.[16] These types of mutations can confer sensitivity to PARPi and inform treatment decisions. The recently presented Phase II ARIEL2 trial investigated the ability of an NGS-based homologous recombination deficiency assay to predict benefit from the PARPi rucaparib in patients with platinum-sensitive, high-grade serous or endometrioid ovarian cancer.[17] Patients with *BRCA*-like tumours, defined by genome-wide loss of heterozygosity due to homologous recombination deficiency, achieved a median progression-free survival (PFS) benefit of 7.1 months, which was intermediate between the 9.4 months for *BRCA*-mutated tumours and 3.7 months for biomarker-negative tumours.

Prof Pujade-Lauraine concluded by emphasising that *BRCA* testing should be utilised in every patient with ovarian cancer. *BRCA* mutations are also found in several other types of cancer, such as breast cancer, pancreatic ductal adenocarcinoma, and prostate cancer.[1] *BRCA* mutation testing is currently recommended for patients with triple-negative breast cancer (TNBC) who are less than 50 years of age.[18] Testing in other tumour types such as pancreatic and prostate cancers is investigational, but could identify patients who may benefit from PARPi.

What Is the Optimal Treatment Approach for *BRCA*-Associated Advanced Ovarian Cancer?

Professor Nicoletta Colombo

Prof Colombo began by asking the audience what first-line treatment they would choose for a 51-year-old patient with Stage IIIC, high-grade serous, *BRCA*-associated ovarian cancer. The responses varied widely, with 43% selecting standard paclitaxel/carboplatin followed by maintenance PARPi and 27% choosing to add bevacizumab to standard chemotherapy with bevacizumab maintenance therapy. Fewer selected standard q3w paclitaxel/carboplatin alone (14%), dose-dense paclitaxel plus carboplatin (10%), or intraperitoneal (IP) chemotherapy (4%).

Prof Colombo commented that q3w paclitaxel plus carboplatin has been the standard first-line therapy for over a decade despite numerous clinical trials investigating substitution or addition of other chemotherapeutic agents.[19] Addition of the antiangiogenic therapy bevacizumab improves PFS and is currently used in Europe as front-line therapy with carboplatin/paclitaxel, followed by maintenance bevacizumab for a total of 15 months.[20-22] IP chemotherapy could also be considered, based on data from the Phase III Gynecologic Oncology Group (GOG) 172 trial showing that *BRCA1*-mutated ovarian cancer was highly sensitive to IP cisplatin/paclitaxel compared with intravenous chemotherapy (median overall survival [OS]: 84.1 versus 47.7 months; p=0.0002).[23] In fact, *BRCA1* mutation was an independent predictor of better survival in patients receiving IP therapy (hazard ratio [HR]: 0.67; p=0.032). Data regarding dose-dense administration of first-line paclitaxel have been conflicting, with one study showing significant benefit in PFS and OS and two similar trials showing no benefit.[24-26] Dose-dense first-line chemotherapy remains a reasonable option, but it is not clear whether this strategy offers a survival benefit.

While many participants indicated that they would recommend PARPi therapy in the front-line setting, Prof Colombo emphasised that this option is not yet approved and would require enrolment in a clinical trial. Several studies evaluating PARPi are underway or planned, including in combination with front-line chemotherapy and/or as maintenance therapy (Table 1). The Phase III SOLO1 trial is comparing the PARPi olaparib versus

placebo as maintenance therapy in patients with *BRCA*-mutated advanced ovarian cancer following front-line chemotherapy;[27] patient accrual is complete and results are eagerly awaited. The ongoing Phase III PAOLA 1 trial randomised patients following first-line chemotherapy to maintenance bevacizumab with either olaparib or placebo.[28] If the SOLO1 and/or PAOLA 1 trials are positive, future selection of front-line therapy for *BRCA*-associated ovarian cancer may include the addition of olaparib as maintenance therapy.

Prof Colombo also asked the participants what second-line therapy they would recommend for platinum-sensitive, *BRCA*-mutated relapse following first-line paclitaxel/carboplatin. The majority selected carboplatin-based chemotherapy followed by olaparib maintenance (44%), although several also felt that a clinical trial of PARPi plus antiangiogenic therapy (22%) or carboplatin/gemcitabine with bevacizumab followed by bevacizumab maintenance therapy (27%) were also reasonable options.

Prof Colombo pointed out that two newly approved options, bevacizumab and olaparib, can now be added to standard second-line, platinum-based therapy. Bevacizumab is approved in combination with carboplatin/gemcitabine as second-line therapy for platinum-sensitive disease based on a significant median PFS benefit over chemotherapy alone in the Phase III OCEANS study (HR: 0.484; p<0.0001).[22,29] There are currently no predictive biomarkers for bevacizumab and it can only be utilised in first relapse. The second option, olaparib, was recently approved in Europe as maintenance therapy for platinum-sensitive, relapsed, *BRCA*-mutated, high-grade serous ovarian cancer based on the results of the Phase II Study 19.[15] Maintenance olaparib showed an impressive improvement in median PFS of 11.2 months compared with 4.3 months for placebo (HR: 0.18; p<0.0001). Olaparib can be given at first or subsequent relapse.

Table 1: Select Phase III clinical trials of PARP inhibitors in ovarian cancer.

PARP inhibitor	Study name	Population	Treatment	Status
Front-line ovarian cancer				
Olaparib	SOLO1	*BRCA1/2*-mutated (+ somatic)	Maintenance	Closed to accrual
Olaparib	PAOLA 1	High-grade serous or endometrioid	Maintenance combination with bevacizumab	Accruing
Veliparib	GOG-3005	High-grade serous carcinoma	Combined with front-line chemotherapy and ± maintenance	Accruing
Niraparib	ENGOT	Adaptive signature for homologous recombination-deficient, high-grade serous carcinoma	Maintenance	Proposed
Recurrent, platinum-sensitive ovarian cancer				
Olaparib	SOLO2	*BRCA1/2*-mutated (+ somatic)	Maintenance	Closed to accrual
Olaparib	SOLO3	*BRCA1/2*-mutated (+ somatic)	Monotherapy versus chemotherapy	Accruing
Niraparib	NOVA	High-grade serous carcinoma or *BRCA1/2*-mutated	Maintenance	Closed to accrual
Rucaparib	ARIEL3	High-grade serous or endometrioid	Maintenance	Accruing
Olaparib	OVM 1403	High-grade serous carcinoma	Olaparib versus olaparib/cediranib versus chemotherapy	Open, not yet accruing
Olaparib	ICON 9	High-grade serous carcinoma	Maintenance olaparib versus olaparib/cediranib	Not yet open

PARP: poly(adenosine diphosphate-ribose) polymerase.
Source: ClinicalTrials.gov

Exciting novel options are also emerging and may change future treatment of platinum-sensitive, relapsed ovarian cancer. For example, the randomised ICON6 trial[30] demonstrated a significant benefit in median OS of 6 months when the antiangiogenic agent cediranib was added to front-line platinum-based chemotherapy and continued as maintenance therapy. This is the first trial to show an OS benefit for antiangiogenic therapy in relapsed ovarian cancer. Another promising strategy is the chemotherapy-free combination of cediranib and olaparib, which recently showed a significant improvement in median PFS of 17.7 months compared with 9.0 months for olaparib alone in a randomised Phase II trial of patients with platinum-sensitive relapsed ovarian cancer (HR: 0.42; p=0.005).[31] Many clinical trials are examining PARPi in platinum-sensitive relapsed ovarian cancer, reflecting the increasing interest in this therapeutic strategy (Table 1).

Prof Colombo summarised by stating that patients with platinum-sensitive, relapsed, *BRCA*-mutated ovarian cancer have several options. Patients can be given gemcitabine/carboplatin with bevacizumab, reserving olaparib for subsequent platinum-sensitive relapse. Alternatively, patients can receive carboplatin-based chemotherapy followed by olaparib maintenance therapy in responders, reserving bevacizumab for subsequent platinum-resistant relapse. Ultimately, participation in clinical trials is always a good option in the front-line and relapsed setting, providing patients access to the best therapies available.

How Should PARP Inhibitors Be Incorporated in Breast Cancer Management?

Professor Andrew Tutt

Prof Tutt opened his presentation with a clinical scenario of a 37-year-old patient with *BRCA1*-mutated TNBC, presenting 8 months after completion of anthracycline and taxane-based adjuvant therapy with asymptomatic recurrence in the liver and supraclavicular lymph nodes. The majority of attendees recommended platinum-based chemotherapy (35%), while 27% chose chemotherapy followed by PARPi maintenance therapy, and 21% chose chemotherapy plus a PARPi. Only 11% and 6% recommended PARPi monotherapy or non-platinum chemotherapy, respectively.

Prof Tutt went on to emphasise the importance of homologous recombination deficiency in the risk of breast cancer. In addition to germline mutations in *BRCA1*, breast tumours themselves can have somatic mutations or promoter methylation of *BRCA1*, as well as mutation of *RAD51C* and other genes involved in regulation of homologous recombination.[32] This results in genomic instability and accumulation of gene rearrangements, insertions, and deletions across the genome, leaving a 'scar' of the homologous recombination defect. Studies are now investigating whether these scars of homologous recombination deficiency, and other biomarkers of homologous recombination defects, may predict potential benefit from platinums and PARPi.

Although platinum chemotherapy is not the current standard of care for breast cancer as a whole, ongoing trials are evaluating platinum-based chemotherapy in specific populations, including *BRCA*-mutated or *BRCA*-like tumours with homologous recombination deficiencies.[33] Prof Tutt described the recently reported results of the Phase III randomised TNT trial comparing carboplatin with docetaxel in patients with advanced TNBC or *BRCA1/2*-mutated breast cancer.[34] While there were no significant differences in the primary endpoint of objective response for carboplatin versus docetaxel in unselected patients with TNBC or in patients with wild-type *BRCA1/2*, those with *BRCA1/2* mutations achieved a doubled objective response rate (ORR) of 68.0% with carboplatin compared with 33.3% with docetaxel (p=0.03). When tumours were classified according to an NGS-based homologous recombination deficiency scar assay, high homologous recombination deficiency scores predicted increased responsiveness to both chemotherapies, not specifically carboplatin. In early-stage TNBC, the Phase II GeparSixto study[35] evaluated non-pegylated liposomal doxorubicin, paclitaxel, and bevacizumab with or without carboplatin. Tumours were tested for *BRCA* mutations and assessed for homologous recombination deficiency scar.[35,36] The addition of carboplatin significantly increased the rate of pathological complete response in patients with TNBC.[35] Similarly to the TNT trial, the presence of a homologous recombination deficiency scar was predictive for higher responsiveness to chemotherapy in both treatment arms and was not specifically predictive for platinum response.[36]

Table 2: Select Phase II/III clinical trials evaluating PARP inhibitors in breast cancer.

PARP inhibitor	Study name	Phase	Population	Treatment	Status
Early-stage breast cancer					
Olaparib	Olympia	III	*BRCA1/2*-mutated TNBC post neoadjuvant or adjuvant chemotherapy	Adjuvant therapy	Accruing
Rucaparib	RIO*	II	Newly diagnosed TNBC or germline *BRCA1/2*-mutated primary breast cancer	Short monotherapy course prior to surgery or neoadjuvant chemotherapy	Accruing
Veliparib	BRIGHTNESS	III	Early-stage TNBC	Neoadjuvant therapy	Accruing
Advanced breast cancer					
Olaparib	OlympiAD	III	*BRCA1/2*-mutated, anthracycline/taxane pretreated ABC	Monotherapy versus physician choice chemotherapy	Accruing
Niraparib	BRAVO	III	*BRCA1/2*-mutated, anthracycline/taxane pretreated ABC	Monotherapy versus physician choice chemotherapy	Accruing
Talazoparib	EMBRACA	III	*BRCA1/2*-mutated, anthracycline/taxane pretreated ABC	Monotherapy versus physician choice chemotherapy	Accruing
Veliparib	M12-895	II	*BRCA1/2*-mutated MBC	Veliparib + temozolomide versus veliparib + carbo/pac versus placebo + carbo/pac	Accruing
Veliparib	NCT02163694	III	*BRCA1/2*-mutated, HER2-negative ABC, first to third-line	Carbo/pac ± veliparib	Accruing

*Rucaparib Window of Opportunity Study. Details available at: http://www.isrctn.com/ISRCTN92154110.
ABC: advanced breast cancer; carbo: carboplatin; MBC: metastatic breast cancer; pac: paclitaxel; PARP: poly(adenosine diphosphate-ribose) polymerase; TNBC: triple-negative breast cancer.
Source: ClinicalTrials.gov

Prof Tutt then pointed out that studies have also demonstrated promising activity for PARPi in patients with *BRCA*-mutated advanced breast cancer, including olaparib, niraparib, and talazoparib.[37] A Phase II trial in *BRCA*-mutated advanced breast cancer demonstrated an ORR of 41% and 22% for two dose levels of olaparib.[38] Interestingly, this efficacy does not appear to extend to the general population of patients with sporadic TNBC, with a Phase II trial enrolling 26 patients with advanced TNBC showing no objective responses to olaparib.[39]

Prof Tutt concluded with a description of ongoing clinical trials evaluating PARPi therapy in breast cancer (Table 2). There is a suite of ongoing Phase III trials comparing the potent PARPi therapies olaparib (OlympiAD), niraparib (BRAVO), and talazoparib (EMBRACA) with standard chemotherapy in patients with *BRCA1/2*-mutated advanced breast cancer resistant to anthracyclines and taxanes.[40-42] PARPis are also being evaluated in combination with non-standard chemotherapeutic agents such as temozolomide or carboplatin/paclitaxel,[43,44] and as neoadjuvant or adjuvant therapy for *BRCA*-mutated early breast cancer.[45-47]

What Are the Implications of PARP Inhibition in Pancreatic and Gastric Cancers?

Professor Eric Van Cutsem

Prof Van Cutsem started his presentation with a clinical scenario, asking participants if they would consider *BRCA* testing for a 57-year-old patient with metastatic pancreatic cancer and a family history of ovarian and breast cancer. Sixty-one percent indicated that they would never or that

they would rarely consider *BRCA* testing for this type of patient, while 20% would test only if they knew there were carriers in the family. Only 20% said that they would always test for *BRCA* mutations.

Prof Van Cutsem then pointed out that pancreatic cancer is a very difficult disease to treat and, despite progress in recent years, there remains considerable room for improvement. DNA damage control is a key signalling pathway involved in pancreatic cancer and represents a novel therapeutic target.[1] Germline *BRCA1/2* mutations are found in approximately 5–7% of patients with unselected pancreatic cancer, with a higher frequency in patients with familial pancreatic cancer and/or an Ashkenazi Jewish heritage.[48] *BRCA2* mutation carriers have a 3.5-fold increased risk of developing pancreatic cancer.[1] Patients with *BRCA* mutations have a median age of diagnosis approximately 10 years younger than the general population, and data suggest a slightly more favourable outcome compared with non-*BRCA*-mutated pancreatic cancer.

Prof Van Cutsem added that while large, randomised data on *BRCA*-mutated pancreatic cancer are lacking, experience at Memorial Sloan-Kettering Cancer Center showed considerable sensitivity to platinum chemotherapy and PARPi in 15 patients with *BRCA1/2*-mutated pancreatic cancer.[49] One patient who received PARPi monotherapy and two of three patients who received PARPi plus chemotherapy achieved a partial response. In addition, five of six patients who received first-line platinum-based chemotherapy responded. A recent Phase II basket trial of olaparib in various advanced cancers also demonstrated promising activity in 23 pretreated patients with *BRCA*-mutated pancreatic cancer, including an ORR of 21.7%, median PFS of 4.6 months, and median OS of 9.8 months.[50] Several ongoing trials are evaluating the role for PARPi in pancreatic cancer, including olaparib, veliparib, and rucaparib in previously untreated or previously treated advanced pancreatic cancer (Table 3).[51-53]

Prof Van Cutsem then discussed the investigation of PARP inhibition in gastric cancer. While the prevalence of *BRCA* mutations in gastric cancer is relatively low, reduced expression of another gene involved in double-strand break repair, ataxia telangiectasia mutated (*ATM*), has been observed in gastric cell lines.[54] ATM expression is low or undetectable in 13–22% of gastric cancer patients, which is associated with shorter survival.[55,56] Interestingly, gastric cell lines with low ATM expression have demonstrated sensitivity to olaparib, creating a rationale for investigation of PARPi.[57]

Table 3: Selected clinical trials of PARP inhibitors in pancreatic cancer.

PARP inhibitor	Study name	Phase	Population	Treatment	Status
Olaparib	POLO	III	*BRCA1/2*-mutated metastatic pancreatic cancer without progression following first-line platinum chemotherapy	Monotherapy maintenance versus placebo	Accruing
Olaparib	NCT01296763	I/II	Advanced pancreatic cancer	Irinotecan, cisplatin, mitomycin C ± olaparib	Closed to accrual
Veliparib	NCT01489865	I/II	Metastatic pancreatic cancer, untreated and previously treated	In combination with modified FOLFOX6	Accruing
Veliparib	NCT01585805	I/II	*BRCA* or *PALB2*-mutated advanced pancreatic cancer, untreated or previously treated	Gemcitabine, cisplatin ± veliparib	Accruing
Rucaparib	RUCAPANC	II	*BRCA1/2*-mutated pancreatic cancer, relapsed disease after 1–2 prior lines of therapy	Monotherapy	Closed to accrual

PARP: poly(adenosine diphosphate-ribose) polymerase.
Source: ClinicalTrials.gov

Prof Van Cutsem described results from a recent Phase II randomised trial comparing paclitaxel/olaparib with paclitaxel/placebo, followed by maintenance olaparib or placebo, in patients with recurrent or metastatic gastric cancer.[54] Patients were tested for ATM expression and the study population was enriched for low or undetectable ATM levels. The addition of olaparib to paclitaxel did not significantly improve median PFS (the primary endpoint). However, olaparib/paclitaxel significantly prolonged median OS in the total patient population (13.1 versus 8.3 months, HR: 0.56; p=0.005) and in the cohort with low ATM expression (not reached versus 8.2 months, HR: 0.35; p=0.002). An ongoing Phase III trial in Asia is further exploring this combination in patients with advanced gastric cancer and disease progression following first-line therapy.[58]

Conclusions

Participants responded to polling questions on PARPi before and after the symposium in order to assess their learning. Attendees demonstrated increased knowledge regarding the role of *BRCA* mutations in prognosis and response to therapy in patients with ovarian cancer, with correct responses increasing from 54% to 80%. Clinicians also demonstrated increased understanding of which types of patients are most likely to have *BRCA* deficiency, including patients with TNBC, high-grade serous ovarian cancer, and pancreatic cancer with a family history. In addition, 90% of participants correctly answered that ATM is a potential predictive biomarker for PARPi sensitivity in gastric cancer, compared with 40% at the beginning of the symposium. Prof Calvert concluded by emphasising that PARPi represent an important innovation in the field of oncology and open the door for other novel therapies inhibiting DNA repair.

Please **click here** to see a webcast of the live meeting.

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