Efficacy of Olaparib in advanced cancers occurring in patients with germline mutations or somatic tumor mutations in homologous recombination genes

A BSMO Precision 2 study

Sofie Joris MD and Jacques De Grève MD, PhD

UZ Brussel

Kom op tegen Kanker

BSMO

AstraZeneca

Second agnostic BSMO sponsored Precision study now open

Precision 2

Efficacy of **Olaparib** in **advanced cancers** occurring in patients with germline mutations or somatic tumor mutations in **homologous recombination genes**

BRCA1/2, ATM, BARD1, BRIP1, CHEK1, CHEK2, MRE11A, NBN, PALB2, RAD50, RAD 51B, RAD51C, RAD51D, RAD54L, FAM175A, CDK12, FANCL, p53 (only germline) and PPP2R2A

Participating Investigators

Marie Martin (CHU Liège), Hannelore Denys (UZ Gent), Tkint de Roodenbeke (IJB), Marika Rasschaert (UZA), Sabine Tejpar (UZ Leuven), François Duhoux (CUSL), Luc Dirix (Iridium network Antwerp), Alain Bols (St-Jan Brugge)

Precision 2 clinical Investigators

Kevin Punie (KUL), Philippe Aftimos (Bordet), Joelle Collignon (CHU Liège), François Duhoux (UCL), Guy Berchem (CH Luxembourg), Marika Rasschaert (UZA), Sylvie Rottey (UZ Gent), Lore Decoster (UZ Brussel)

Genetic cancer clinicians (BSMO working party on genetic cancer)

Marie Martin (CHU Liege), Christos Sotiriou (IJB), Alain Bols (St-Jan Brugge), Hannelore Denys (UZ Gent) Christel Fontaine (UZ Brussel), Tkint de Roodenbeke (IJB), Olivier Bechter (KU Leuven), Luc Dirix (Iridium network Antwerp)

Genetics Labs

Kathleen Claes (UZ gent), Gert Matthys (KUL),
Alexander Geldhof (VUB), Vincent Bours (ULiege)

Financial support

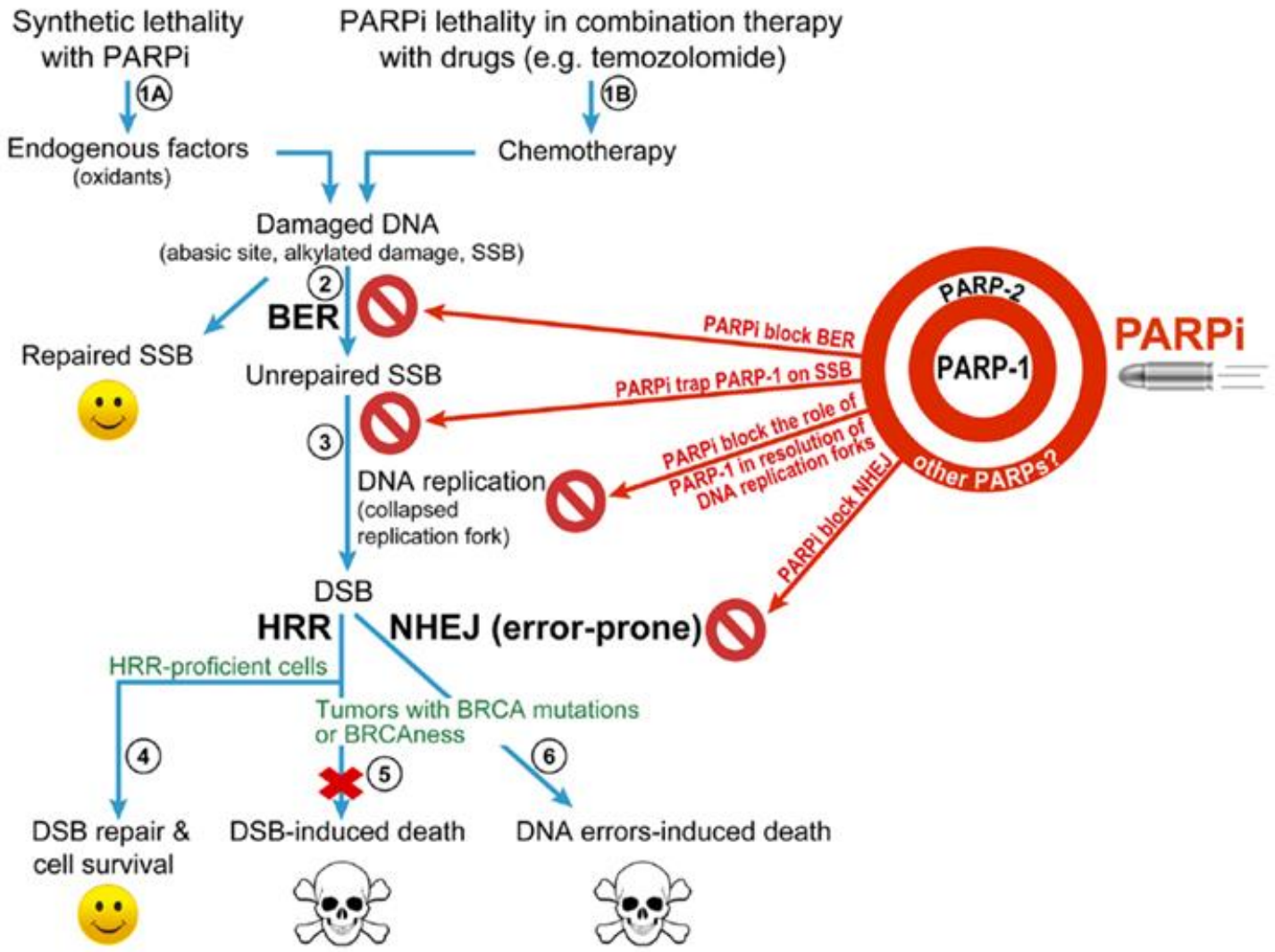
Kom op tegen Kanker

Stichting tegen Kanker
Fondation contre le Cancer

Rationale and purpose

- Targeted therapy with the **PARP inhibitor olaparib** has become standard of care in **advanced platinum sensitive BRCA1/2 mutant ovarian cancer**
- The key in this sensitivity is the **loss of homologous recombination (HRD) function**
- **Many genes can lead to HRD**
- The current project aims to treat patients with any type of cancer carrying in their **germline** a mutation in **genes** that generate such an **homologous recombination deficiency** (HRD) or have an acquired **somatic** mutation in their tumor with the targeted PARP inhibitor olaparib

Mechanism



Shah GM et al, Front Oncol. 2013; 3: 279

Primary objective

Document **anti-tumor activity** (measured by response rate and response duration) of olaparib in advanced cancer patients that have a germline mutation or a somatic tumor mutation among a defined list of HR genes

Study population

- **Advanced cancer patients** that have a **germline** mutation or a **somatic mutation** in **HR genes**. Ovarian cancer patients harboring a HRD and breast cancer patients who carry a BRCA1/2 mutation will be excluded. All other cancer types with a homologous recombination deficiency (HRD) will be eligible.

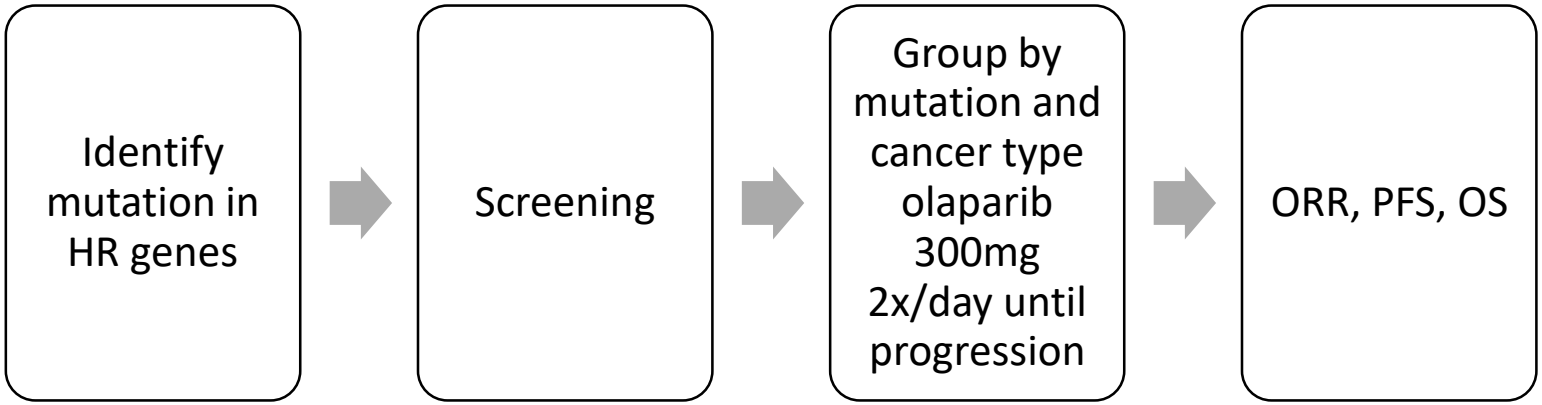
- 540 patients can enter in the study for the genetic driven cohorts (optimal Simon 2 stage design)
  - 13 patients will be enrolled per cancer type in the first stage and an additional 14 in the second stage.

Methods

- Academic, multicenter, multi-cohort, explorative phase II basket study

- HR genes:
  BRCA1/2, ATM, BARD1, BRIP1, CHEK1, Chek2, MRE11A, NBN, PALB2, RAD50, RAD51B, RAD51C, RAD51D, RAD54L, FAM175A, CDK12, FANCL, p53 and PPP2R2A

Study design



Project status 29/01/2020

Study Protocol	Site n°-PI	N° of patient screened	N° of patient screened but not eligible	N° of patient randomized											N° of patient completed
				RAD51C	RAD51D	Check 2	BRCA1	BRCA2	HER2	CDKN2A	ATM	PALB2	BAP1	HER3	
Precision-2: Olaparib	01-Dr. Joris	8		1	1	1	3	1				1			3
	02-Prof. Denys	3						2					1		
	03-Dr. Collignon	1						1							
	04-Dr. Rasschaert														
	05-Dr. T'Kint de Roodenbek	1				1									
	06-Prof. Duhoux														
	07- Prof. Tejpar	7	1				2	2			1	1			
	08-Dr. Dirix														
	09-Dr. Bols														
	10-Dr. Canon														
	11-Dr. Mebis														
	12-Dr. Berchem														
		20	1	1	1	2	5	6	0	0	1	2	1	0	


THANK YOU
THANK YOU
THANK YOU
THANK YOU
THANK YOU
THANK YOU
THANK YOU
THANK YOU