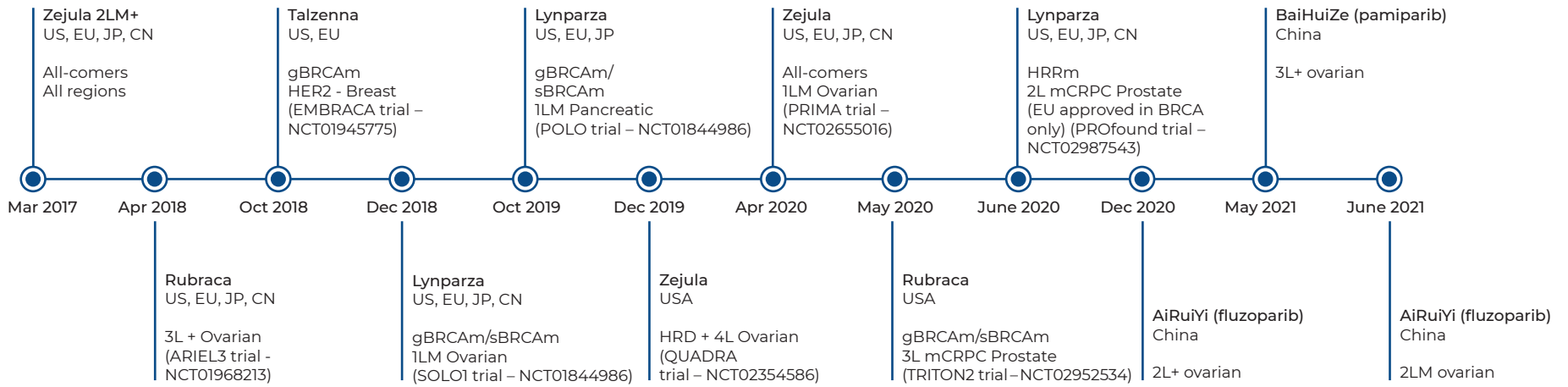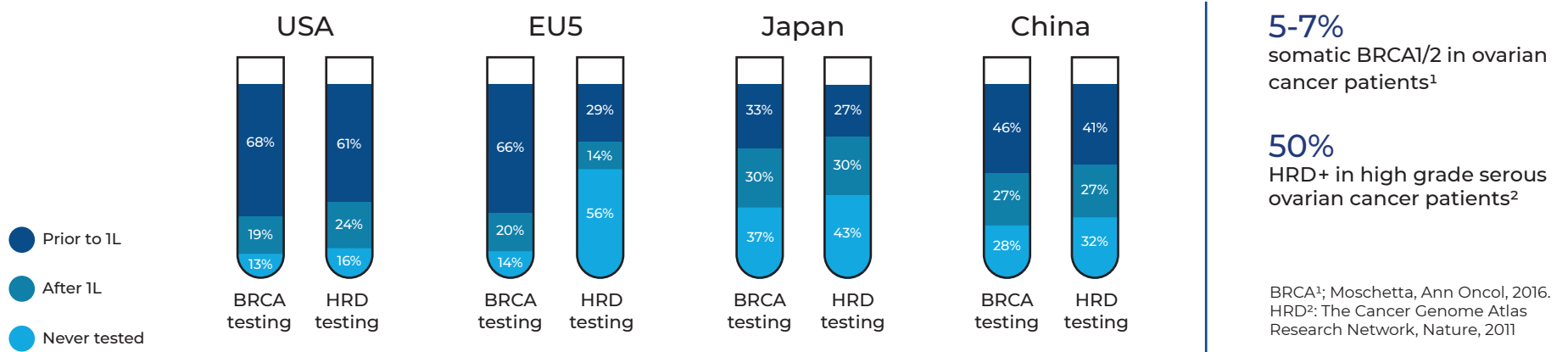# Better testing, better outcomes in Rare Cancer:
BRCA mutation and PARP inhibitors

Patients whose tumors have mutations to homologous recombination repair genes, which include BRCA1 and BRCA2, may be homologous recombination repair deficient (HRD) due to genomic instability. Ovarian tumors that are HRD and/or have BRCA1 or BRCA2 mutations may be sensitive to a class of drugs called PARP inhibitors.

*Timeline has been simplified with dates shown for initial US approvals, with the exception of AiRuiYi and BaiHuiZe, which are only approved in China

Timeline (above line):

- **Mar 2017** — Zejula 2LM+ / US, EU, JP, CN / All-comers / All regions
- **Oct 2018** — Talzenna / US, EU / gBRCAm / HER2 - Breast (EMBRACA trial – NCT01945775)
- **Oct 2019** — Lynparza / US, EU, JP / gBRCAm/sBRCAm / 1LM Pancreatic (POLO trial – NCT01844986)
- **Apr 2020** — Zejula / US, EU, JP, CN / All-comers / 1LM Ovarian (PRIMA trial – NCT02655016)
- **June 2020** — Lynparza / US, EU, JP, CN / HRRm / 2L mCRPC Prostate (EU approved in BRCA only) (PROfound trial – NCT02987543)
- **May 2021** — BaiHuiZe (pamiparib) / China / 3L+ ovarian

Timeline axis: Mar 2017 | Apr 2018 | Oct 2018 | Dec 2018 | Oct 2019 | Dec 2019 | Apr 2020 | May 2020 | June 2020 | Dec 2020 | May 2021 | June 2021

Timeline (below line):

- **Apr 2018** — Rubraca / US, EU, JP, CN / 3L + Ovarian (ARIEL3 trial - NCT01968213)
- **Dec 2018** — Lynparza / US, EU, JP, CN / gBRCAm/sBRCAm / 1LM Ovarian (SOLO1 trial – NCT01844986)
- **Dec 2019** — Zejula / USA / HRD + 4L Ovarian (QUADRA trial – NCT02354586)
- **May 2020** — Rubraca / USA / gBRCAm/sBRCAm / 3L mCRPC Prostate (TRITON2 trial – NCT02952534)
- **Dec 2020** — AiRuiYi (fluzoparib) / China / 2L+ ovarian
- **June 2021** — AiRuiYi (fluzoparib) / China / 2LM ovarian

BRCA mutation testing in ovarian cancer is becoming more common, since PARP inhibitors are approved globally for ovarian cancer; but HRD testing occurs less often.

	USA		EU5		Japan		China	
	BRCA testing	HRD testing	BRCA testing	HRD testing	BRCA testing	HRD testing	BRCA testing	HRD testing
Prior to 1L	68%	61%	66%	29%	33%	27%	46%	41%
After 1L	19%	24%	20%	14%	30%	30%	27%	27%
Never tested	13%	16%	14%	56%	37%	43%	28%	32%

5-7% somatic BRCA1/2 in ovarian cancer patients[1]

50% HRD+ in high grade serous ovarian cancer patients[2]

BRCA[1]; Moschetta, Ann Oncol, 2016.
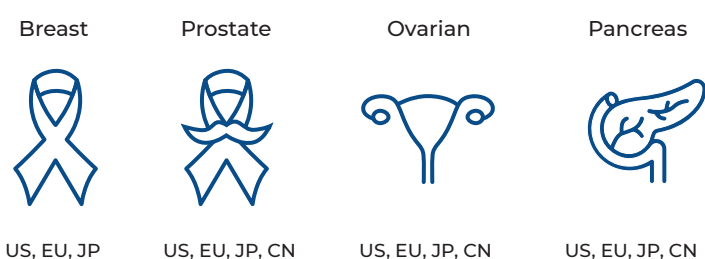HRD[2]: The Cancer Genome Atlas Research Network, Nature, 2011

Patients who have BRCA mutations or are HRD positive usually receive 1st line chemotherapy and then a PARP inhibitor as maintenance therapy which can keep tumors at bay for many months.

Cancer cells → Chemotherapy → PARP inhibitor stops tumor from growing → More time cancer free
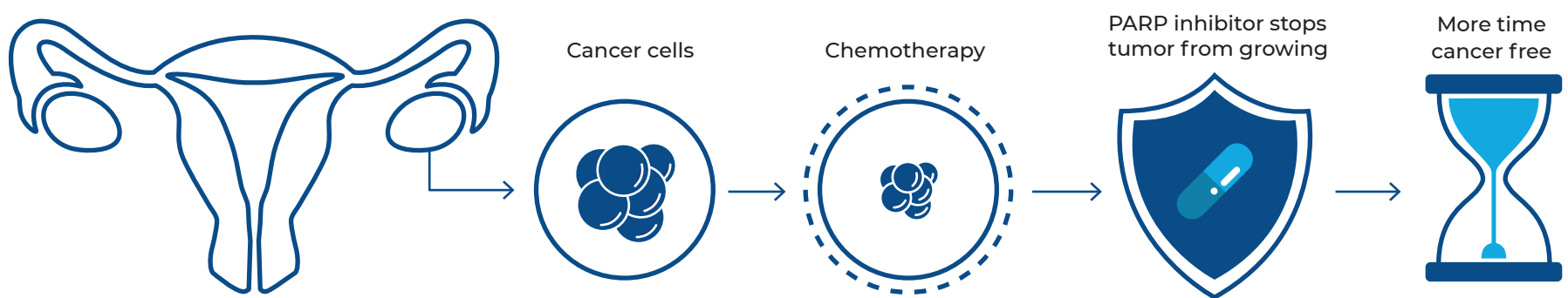
Ovarian cancer patients were the first to benefit from treatment with PARP inhibitors based on the genetic abnormalities in their tumors, but many cancers have BRCA mutations or are HRD. Some patients with other solid tumors already have PARP inhibitors available to help treat their cancers; and there is opportunity in others.

Tumors with PARP approvals

- **Breast** — US, EU, JP
- **Prostate** — US, EU, JP, CN
- **Ovarian** — US, EU, JP, CN
- **Pancreas** — US, EU, JP, CN

Phase 3 development

- Uterine
- NSCLC (non-small cell lung cancer)
- Colorectal
- SCLC (small cell lung cancer)

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