WORKING GROUP

Clinical study in patients with stage IV non-small cell lung cancer

Background information
The disease

- Non-small cell lung cancer (NSCLC) accounts for approximately 80% of lung cancer cases. The majority of these cases present with unresectable locally advanced (stage IIIB) or metastatic disease (stage IV) at diagnosis.

Background information

The therapy

- The initial treatment for inoperable NSCLC is platinum-based doublet chemotherapy. Among these regimens, gemcitabine/cisplatin (GC) is widely used and is approved by health authorities in Europe.

- A phase 3 trial with 863 NSCLC patients treated with GC[1]:
  - An overall survival of 10.3 months (1-year survival rate, 41.9%)
  - A progression free survival (PFS) of 5.1 months
  - An objective response rate (ORR) of 28.2%

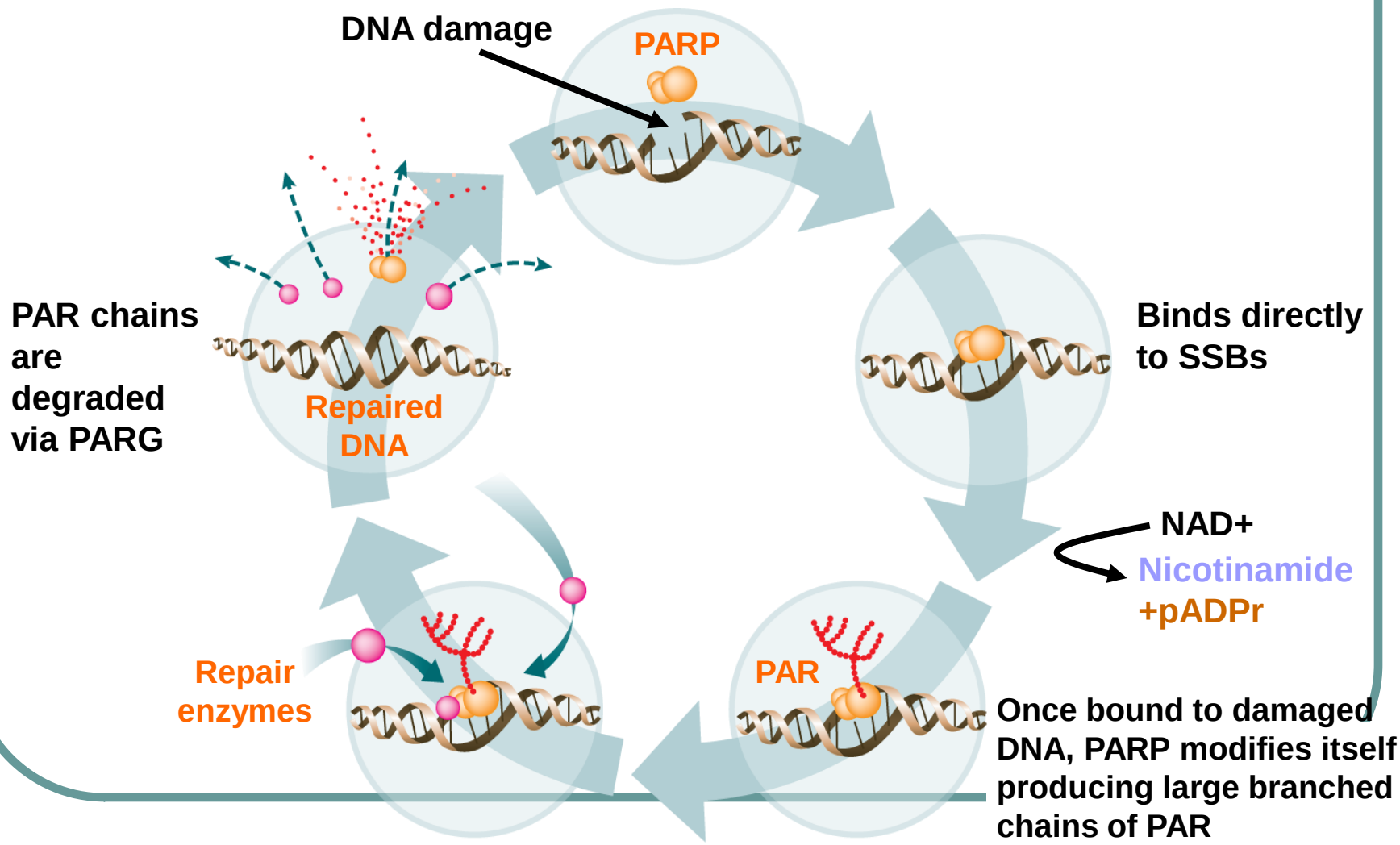
- Nevertheless, these results are not satisfactory and newer agents able to target specific steps of cancer cells proliferation are strongly needed.

1. Scagliotti GV et al J Clin Oncol. 2008; 26(21):3543-3551

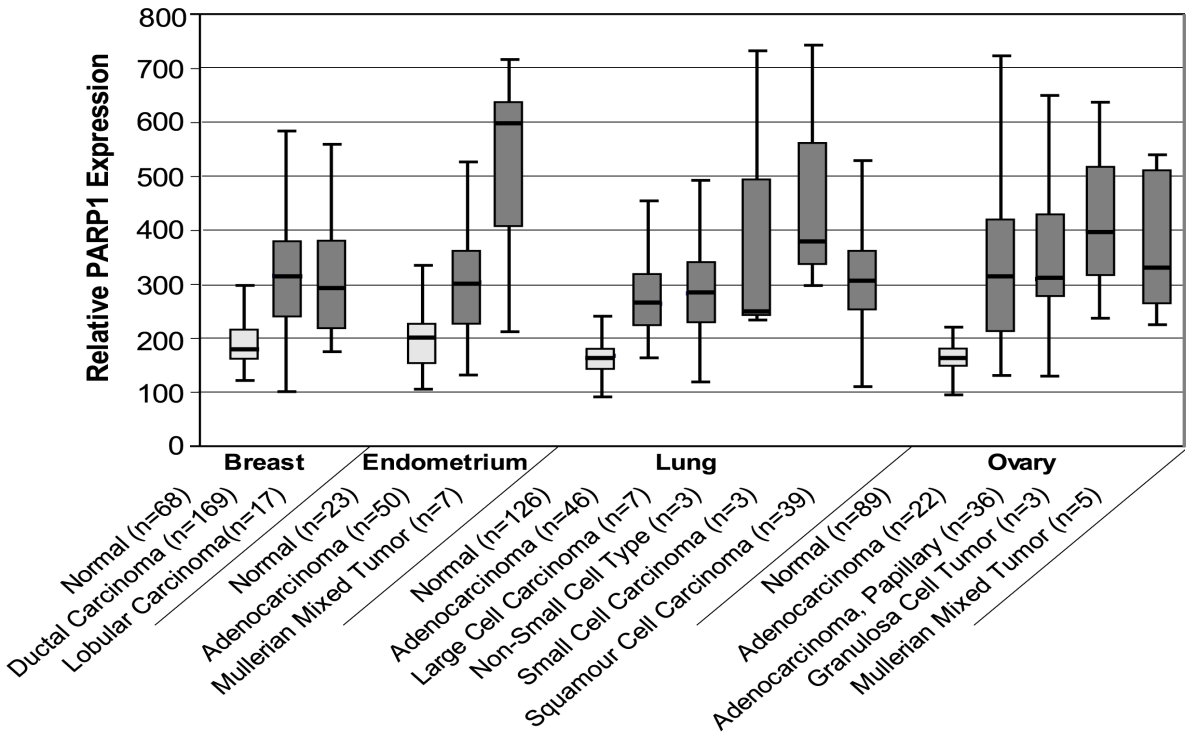
New drug

- The new drug is a small molecule (MW<300) that inhibits the activity of poly (ADP-ribose) polymerase (PARP);
- Short half-life;
- Lipophilic;
- Penetrates blood brain barrier;
- Administration: IV;
- Well tolerated.

PARP and structure based drug design



Increased PARP1 gene expression in human primary cancers



New drug + CT

- Observed synergy between the new drug and gemcitabine or carboplatin in a preclinical study.
- No potentiation of chemotherapy-related toxicities observed when combined with gemcitabine/carboplatin.
- New drug used in TNBC (phase 2 and 3 studies) in combination with gemcitabine/carboplatin:

  5.6 mg/kg I.V. twice weekly (days 1, 4, 8 and 11)

Study protocol

- Background and rational
- Study Objectives
- Primary and secondary endpoints
- Study design
- Inclusion and exclusion criteria
- Study treatments + dose delays and dose reduction
- Assessment of investigational product
- Patient safety
- Study procedures and visit schedule
- Statistical considerations