STAMP Working Group on repurposing - Objective 2

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Goals of objective 2

- To provide **‘real life’ examples** of product(s) / indications that could have been put through the pathway
- To consider how a **pilot** for testing the repurposing pathway might be introduced

Template for collecting information

- **Available product information:** Active substance, authorised indication(s), authorised dosage form(s), authorisation details (MAHs, countries, etc.)
- **New therapeutic use:** Proposed indication, unmet medical need or significant public health benefit
- **Potential incentives:** Regulatory incentives (e.g. ODD, PUMA), IP (e.g. second and further medical uses), other incentives (e.g. H2020 and other grants, support from patient groups)
- **Evidence: (**Non-clinical data), clinical trial data and case reports, real world data (post-authorisation studies, registry data), information from clinical treatment guidelines

Case 1: Example of late entry into the pathway

Docetaxel in hormone sensitive metastatic prostate cancer

- Data available from three Phase III trials (STAMPEDE, CHAARTED and GETUG-AFU 15 trial)
- Two phase III trials are still ongoing (PEACE-1 and ARASENS trial)
- Studies with real-world evidence
- Off-label use is common (ESMO Clinical Practice Guidelines, European Association of Urology prostate cancer guidelines, NCCN Prostate Cancer Guidelines)

→ Need for **guidance** on how to deal with (contradictory) results from clinical trials and RWE-studies.

Case 2: Example of early entry into the pathway

CUSP9v3 protocol in recurrent glioblastoma

- Phase 1 trial nearly completed with positive results (combination appears to be safe).
- Liaising with all involved MAHs would be very complicated for the champion.
- Unclear what regulatory pathway should be followed to bring this combination on-label. Medicines would be administered in same dosage form as specified in original MA.

→ Need for **early scientific advice** on regulatory and scientific challenges.

Learnings from the case studies

- A **single entry** point into the pathway lowers the threshold for champions to send in a proposal.
- Gathering data on the authorisation details of an active substance might be quite challenging for a champion. The **Article 57 database** published by the EMA on their website provides an up-to-date overview of all MAHs for an active substance authorised in Europe. The link to the Article 57 database could be included in the template/check list for the champion.
- Preparing a data package for a scientific advice meeting is challenging for a champion with limited knowledge of the regulatory process. **Guidance documents and a template/topic checklist** would be useful.

Learnings from the case studies

- The pathway should allow **combinations of repurposed drugs** (e.g. CUSP9v3 combination of nine repurposed drugs with temozolomide).
- The case of docetaxel showed that **data from multiple phase 3 trials and real-world evidence studies** might be available. Therefore, champions should provide an exhaustive list of all available data, even if these data seem to be contradictory. This is an unexpected complexity since a MA for a new medicine is based on a single registration trial.
- A lot of time and effort would be required from the champion. Their efforts should be rewarded by **removing certain disincentives**, like the cost of SA.

Suggestion for pilot cases

Late-stage development:

- Adjuvant bisphosphonates for the prevention of breast cancer spreading to the bone in post-menopausal women with primary breast cancer
- A lot of evidence to support off-label use, off-label use is common

Early-stage development:

- Propranolol in cutaneous angiosarcoma
- ACF has an ODD in this indication and is preparing a dossier to apply for protocol assistance by EMA

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ReDO_DB: the repurposing drugs in oncology database

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Abstract

Repurposing is a drug development strategy that seeks to use existing medications for new indications. In oncology, there is an increased level of activity looking at the use of non-cancer drugs as possible cancer treatments. The Repurposing Drugs in Oncology (ReDO) project has used a literature-based approach to identify licensed non-cancer drugs with published evidence of anticancer activity. Data from 268 drugs have been included in a database (ReDO_DB) developed by the ReDO project. Summary results are outlined and an assessment of clinical trial activity also described. The database has been made available as an online open-access resource (http://www.redo-project.org/db/).

Research

Questions?

Anticancer Fund