GENEQOL Consortium meeting

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EORTC HQ
Brussels, Belgium
Private non-profit organization created in 1962 (47 years old)

Core activity: conduct of clinical trials
- International
- Multidisciplinary
- Define new standards of care
- Large academic trials, mostly in large academic centers/hospitals
  - Phase I
  - Phase II
  - Phase III
  - Feasibility trials
EORTC Structure

EORTC HQ
Brussels, including QOL Department

Breast
Lung
Lymphoma
Genito-Urinary
Brain
Gastrointestinal
Melanoma
Head & Neck
Gynecological
Leukemia

Coordinates the scientific activities of the EORTC Groups

5,000 patients enrolled into clinical trials each year

90%
Europe
10%
Rest of the world

2,500 clinicians in 33 countries

Since 1980 some 140 HRQOL clinical trials with HRQOL activated
Request for trials suitable for GENEQOL

- Contain QoL & tissue microarray data.

- Rare combination
  - QoL mainly in phase III trials: large & comparative RCTs where QoL is secondary endpoint.
  - TMA mainly in phase II trials: small & intensive trials where TMA is exploratory research.

- In phase III tumour tissue collection exists but:
  - Often linked to a specific marker (eg. P53, EGFr expression, methylation status, ...) not to construct complete TMA.
3 main options

1. Trials with QoL and extensive TR foreseen in protocol.
2. Trials with QoL and publicly available TMA database.
3. Trials with QoL and external/optional TR.
Completed trials:

- **EORTC-24971**: A randomized phase III multicenter trial of neoadjuvant docetaxel (Taxotere) plus cisplatin plus 5-fluorouracil versus neoadjuvant cisplatin plus 5-fluorouracil in patients with locally advanced inoperable squamous cell carcinoma of the head and neck
  - 358 patients
  - Status: study results published. Tumour tissue collected but TMA construction project on hold due to insufficient funding. Discussion with sponsor ongoing.

- **EORTC-26981**: Concomitant and adjuvant Temozolomide and Radiotherapy for newly diagnosed glioblastoma multiforme. A randomized phase III study
  - 520 patients
  - Status: study results published. Tumour tissue collected and methylation status assessed. Further TMA construction project on hold due to insufficient funding.
Completed trials:

- EORTC-18032: Extended schedule, escalated dose Temozolomide versus Dacarbazine in Stage IV Metastatic Melanoma: A Randomized Phase III Study of the EORTC Melanoma Group
  - 859 patients.
  - Status: study results in press. MGMT depletion and DNA methylation in tumour and peripheral blood mononuclear cells assessed. No further plans for TMA construction currently.
Trial overview – option 1

Ongoing trials

- EORTC-55041: A randomized, multicentre, phase III study of Erlotinib versus observation in patients with no evidence of disease progression after first line, platinum-based chemotherapy for high-risk Stage I and Stage II-IV ovarian epithelial, primary peritoneal, or fallopian tube cancer
  - 832 patients
  - Planned TR = egfr mutations (introns 18, 19, 21); PI3K mutations; Polymorphisms in egfr intron 1 CA repeats.
  - Expected availability = end 2010.

- EORTC-22991: Three Dimensional Conformal Radiotherapy / Intensity Modulated Radiotherapy alone vs Three Dimensional Conformal Radiotherapy / Intensity Modulated Radiotherapy plus adjuvant hormonal therapy in localized T1b-c, T2a, N0, M0 prostatic carcinoma. A Phase III Randomized Study
  - 800 patients – TR optional
  - Planned TR: TMA feasibility study
  - Expected availability = end 2013
Trial overview – option 1

Ongoing trials

- **EORTC-22071**: Randomized Phase III trial on postoperative chemoradiation in combination with anti EGFR-antibody versus postoperative chemoradiation in head and neck squamous cell carcinomas (HNSCC) with high risk of locoregional recurrence
  - 800 patients
  - Planned TR: TMA construction
  - Expected availability = end 2016

- **EORTC-22043**: Post-operative external radiotherapy combined with concomitant and adjuvant hormonal treatment versus post-operative external radiotherapy alone in pathological stage pT3a-b R0-1/pT2R1 N0M0, Gleason score 5-10 prostatic carcinoma. A phase III study
  - 600 patients
  - Planned TR: TMA on predetermined markers: TMPRSS2-ERG fusion, EZH2:ECAD status, PTEN loss, pAkt, CAG/GGC repeats lengths on AR gene
  - Expected availability = mid 2017
EORTC trials with publicly available TMA data

- 3 trials could be identified (2 breast, 1 melanoma)
- None contained QoL data.
• Trials with QoL and external/optional TR.
• Many trials contain tumour sampling
• These samples can then be used later for further research (ie. research not initially foreseen in the study protocol).
• This type of research is not initiated by EORTC itself but by a third party (research consortium, academia, industry, …)
• Is dependent on a review by EORTC for scientific interest/quality, tumour availability and patients’ informed consent.
Problem:

These external research projects were not collected in a uniform method (only recently there is a standard procedure for tracking these projects).

Selecting appropriate projects is a manual task.

Involves getting agreement from 2 parties

- clinical & QoL data: EORTC
- TR data: external party
Conclusion

- EORTC has large archives
  - … but very few suitable trials. Mainly due to the phase II / phase III split.
- Large trials with QoL and TMA are currently being set up but these will not be available for several years.
- Note:
  - release of data is subject to an “external research project” review. (Bureaucratic exercise)
  - Release of TR data is subject to review of patients’ informed consent
    - Patients can opt in or out of “future use of their tissue material”. (trial dependent)
    - TR data would only available for patients who consented for future use. In some trials this is only a fraction of the total available patients.