



Procedure for Access to Biological Materials and Genomic / Clinical Data in the ALTTO Trials

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1. Introduction

The ALTTO Trials (comprising of **both** the ALTTO study and the NeoALTTO study) sponsored by GlaxoSmithKline (GSK), and conducted under the auspices of the Breast International Group (BIG) will collect and store biological materials for the purpose of correlative science research. North Central Cancer Treatment Group (NCCTG) is a partner for the ALTTO study and SOLTI is a partner for the NeoALTTO study. These materials will be available for research as outlined in the ALTTO Trials' Protocols, as well as for new research that may be proposed by investigators affiliated with the ALTTO Trials and by the wider scientific community.

A strict review process of translational research proposals exists to ensure precious biological materials and genomic / clinical data collected in the ALTTO Trials are accessed appropriately. This procedure provides the guidelines for the review and approval of such translational research proposals.

This procedure does NOT cover

- Translational research studies that are already part of the ALTTO Trials' Protocols
- Translational research studies that do not require bio-specimens

2. General Principles

1. Biological Materials

Available biological materials which are collected within the ALTTO Trials include; tissue microarrays (TMAs, paraffin embedded tumour samples), snap frozen tumour tissue for proteomics and gene expression analyses, RNA/DNA extraction as well as blood for circulating tumour cells and proteomics.

2. Custodianship and governance

These materials are stored under the custodianship of the ALTTO Trials' Steering Committee (SC) in various independent facilities specified by the relevant clinical trial documents. The SC is the ultimate governing body of the ALTTO Trials.

The TransALTTO Committee functions under the governance of the SC, and is an expert body that reviews translational research proposals for scientific merit and feasibility, and makes recommendations to the SC for final approval. In addition, the TransALTTO Committee acts as an advisory body to the SC for other important translational issues that may affect the conduct of the ALTTO Trials.

In special circumstances, the SC can delegate final approval of research proposals to the ALTTO Trials' Executive Committee (EC) which is a sub-committee of the SC, responsible for rapid decision-making. In this case, the approval shall require a decision of the full EC, endorsed by the SC.

3. Types of translational research proposals

- a) Internal proposals: These are proposals made by individuals who have contributed to the ALTTO Trials in any form or manner, and can include Investigators and TransALTTO Committee members.
- b) External proposals: These are proposals made by individuals from the wider scientific community not involved with the ALTTO Trials.

All internal and external proposals will be reviewed by 2 TransALTTO Committee members and one of the ALTTO Trials' statisticians, who are independent from the proposal, and 1 external scientific reviewer appointed by the TransALTTO Committee Chairs. Proposals deemed as high

priority by the TransALTTO Committee that use North American Cooperative Groups' specimens will be submitted to National Cancer Institute (NCI) for additional scientific review.

4. Eligibility for review

All project proposals, in addition to presenting outstanding scientific merit, must

- Specify exactly what types and amount of data and / samples are needed, based upon the proposed analysis and the statistical rationale
- Be compatible with all of the ALTTO Trials' contractual commitments, and policies related to confidentiality (see point 2.6) and publication (see point 2.9)
- Be self-funded and include a detailed budget with description of potential funding sources. The budget MUST include overhead costs incurred for coordinating the review process.

5. Additional Ethical – legal review

For both internal and external proposals, which are scientifically sound, but requiring additional ethical-legal advice (as decided by the scientific reviewers), ethical-legal experts will be appointed.

6. Confidentiality

The content of all project proposals must be kept confidential by all TransALTTO Committee reviewers, statistical reviewers and by all external reviewers (scientific and ethical-legal).

7. Contractual Commitments

All projects will have a contract with BIG and will detail data ownership, intellectual property right (IPR), publication, possible exploitation issues and budget.

8. Left-over biological material

After completion of the approved research project, all left over biological materials will need to be returned to the relevant tissue repository where it was received from. Only with permission from the SC can left-over material be destroyed or stored in the Investigator's laboratory. Any additional usage of the left-over material, beyond the initial proposal, must undergo another review process and be approved by the SC.

9. Publications / Presentations

Refer to the "*ALTTO Publication Guidelines*" for full details. Until the public presentation and/or publication of the results of the primary endpoint of the ALTTO Trials, any release of data must have the prior approval of the Independent Data Monitoring Committee (IDMC) and the SC.

All projects must acknowledge the ALTTO Trials Study Team in all presentations and publications. Acknowledgement of particular individuals may be requested on a case by case basis.

3. **Procedure**

1. Internal and external proposals requiring bio-specimens for translational research, not already included in the ALTTO Trials' protocol, should be submitted to the Proposals Coordinator at Frontier Science (transaltto@frontier-science.co.uk).
2. All proposals will be reviewed for initial feasibility by the TransALTTO Committee Chairs (assessed according to point 2.4).
3. If a proposal is deemed suitable for formal review, the TransALTTO Committee Chairs will appoint scientific reviewers (from the TransALTTO Committee and external reviewers). All scientific reviewers

will be provided with scoring guidelines. All proposals will undergo review by one of the ALTTO Trials' statisticians.

4. Proposals that are not deemed suitable for formal review should be included in the report to the SC.
5. Additional ethical-legal review may be requested from the scientific reviewers, in which case appropriate experts will be appointed by the TransALTTO Chairs.
6. After receiving evaluations from the panel of scientific (+/- ethical-legal) reviewers, the TransALTTO Committee members will be able to vote, rank and prioritise all proposals received during an evaluation period (according to voting guidelines outlined in the *TransALTTO Committee Guidelines*). The TransALTTO Committee will convene at regular and pre-specified intervals, either electronically, by teleconference or in face-to-face meetings, to facilitate the voting process of research proposals.
7. The TransALTTO Committee Chairs will submit and present a summary of the evaluated proposals, a suggested decision (approve / reject) and a priority for implementation to the SC. All proposals rejected based on feasibility, contractual, legal or IPR grounds will also be communicated to the SC.
8. The SC will vote based on the recommendations of the TransALTTO Committee, and according to the voting guidelines described in the *SC Guidelines*.

4. Practicalities

The following steps are involved in the proposal submission

1. Applicants must complete a '(Neo)ALTTO Research Project Proposal Submission Form' (for NeoALTTO or ALTTO samples as appropriate) providing all required information, and submit the proposal to Frontier Science according to the instructions on the form.
2. Evaluation periods for proposals will be organized on a 6-monthly basis and will be made publicly available.
3. The TransALTTO Committee will convene every 6 months (either electronically, by teleconference or in face-to-face meetings) to vote, rank and prioritise proposals
4. After proposal submission the review process is then carried out (as per section 3)
5. The SC will provide the final vote on research proposals. The SC, under special circumstances, can delegate the final voting to the EC during their more frequent meetings, if requested by the TransALTTO Committee Chairs. Such special circumstances could include the unexpected backlog of proposals, or an extraordinary proposal requiring rapid decision-making.
6. Applicants will, in general, receive a final response regarding the evaluation of their proposal within 3 months after the deadline of a given evaluation period.
7. Conditional approval given by the SC will be for a period of 6 months, during which time the applicant must secure funding as outlined in the budget submitted in the proposal. Any request for an extension to the conditional approval will be considered on a case-by-case basis only.
8. Proposals that are not approved may be re-submitted to address the concerns and comments raised during the review process for a final decision.