European Thoracic Oncology Platform
History

- April 2008 1st European Lung Cancer Congress Geneva: formal structure needed to promote collaboration
- May 2008: Paul Baas and Rolf Stahel discuss structure based on modified IBCSG documents
- September 08 ESMO Stockholm: 1st ETOP meeting with presentation and acceptance of concept, suggestions for members of foundation council, initiation of collection of funds by interested groups and institutions
- January 09 BTOG Dublin: First meeting of foundation council, approval of charter and bylaws
- May 09: approval of foundation by authorities and acceptance by trade registry of Bern
3rd ETOP meeting November 2010

• SPLENDOUR
• NICHE
• BELIEF
• Lungscape
• iBiobank
The European Thoracic Oncology Platform (ETOP) is a foundation with the purpose to promote exchange and research in the field of thoracic malignancies in Europe.

Aims:

• To serve as a meeting platform for European study groups and institutions dealing with thoracic malignancies
• To foster intergroup studies among, but not exclusively, European study groups and institutions
• To sponsor and/or perform own studies
• To foster scientific exchange on laboratory and clinical issues among interested parties and beyond
• To provide knowledge to partners in the field
Structure and Committees

Not-for-profit foundation under Swiss law (President: Rolf Stahel, Zurich)

• Foundation Council → charter and bylaws
• Scientific Committee (Chair: Rolf Stahel, Zürich)
• Scientific Coordinator (Solange Peters, Lausanne)
• Independent Data Monitoring Committee → IDMC guidelines
• Trial specific Steering Committees → Steering Committee guidelines

Other committees as appropriate
Foundation council and scientific committee

Foundation council
• Rolf Stahel, Switzerland (President)
• Paul Baas, Netherlands
• Keith Kerr, United Kingdom
• Sanjay Popat, United Kingdom
• Rafael Rosell, Spain
• Suresh Senan, Netherlands
• Solange Peters, Switzerland
• Walter Weder, Switzerland
• Christoph Zielinski, Austria
ETOP Group Offices

• ETOP Office Zürich
• ETOP Coordinating Office Bern
• ETOP Scientific Coordinator Lausanne
• ETOP Statistical Office Athens
Trial concept development, funding and conduct:

• Concept ideas from ETOP leadership, ETOP Principal Investigators, or associated researchers. Proposal outline including study drug, design, population, short rationale, objectives and most important inclusions and exclusion criteria to be sent to ETOP for evaluation

• Statistical considerations, budget setup and contacts with pharmaceutical companies are responsibilities of ETOP

• Feasibility survey among ETOP network

→ Protocol development by ETOP leadership, Study Chair(s) and trial operations team
Trial Operations

Coordinating Office Bern, Switzerland
(ETOP Director: Anita Hiltbrunner):

• Protocol development, project management and supervision, coordination of reporting and dissemination of results
• Data management
• Regulatory affairs
• Pharmacovigilance
• Medical review and expertise
• Quality assurance
• Quality control: on-site and remote monitoring
• Coordination of biobanking and translational research
• Group management and finances
• General administrative and technical services, e.g. insurance
Trial Operations

Statistical Office Athens, Greece (Director: Urania Dafni):
- Trial design
- Sample size calculations
- Randomization
- Data analysis
- Reporting

Instruments:
- ICH guidelines (GCP)
- Standard Operating Procedures SOPs and work instructions
- Database: ETOPdata
- Publication guidelines
- Biobank policy
ETOP Coordinating Office Bern – The Entire Team
Austria
- CECOG – Central European Cooperative Oncology Group
- Translational Thoracic Oncology Lab

Belgium
- ELCWP – European Lung Cancer Working Party
- EORTC Lung Cancer Group
- Oncologisch Centrum UZ Brussel
- Thoracic Oncology Unit, Department of Pulmonary Diseases, Heilig Hart Ziekenhuis Roeselare
- TOGA – Thoracale Oncologie Groep Antwerpen

Czech Republic
- Czech Lung Cancer Cooperative Group

Denmark
- DLCG – Danish Lung Cancer Group
- DOLG – Danish Oncological Lungcancer Group

Finland
- Finnish Lung Cancer Study Group

France
- GFPC – Groupe Français de Pneumo-Cancérologie
- ICO – Integrated Centers of Oncology
- IFCT – Intergroupe francophone de Cancérologie thoracique
- IGR – Institut Gustave Roussy

Germany
- AOT – Arbeitsgemeinschaft Onkologische Thoraxchirurgie
- Arbeitsgruppe Thorakale Onkologie der Arbeitsgemeinschaft Internistische Onkologie der Deutschen Krebsgesellschaft
- Lung Cancer Group Cologne
- Pius-Hospital Oldenburg
- Thoraklinik am Universitätsklinikum Heidelberg

Greece
- HeCOG – Hellenic Co-operative Oncology Group
- HORG – Hellenic Oncology Research Group
- Oncology Unit GPP, Athens School of Medicine

Hungary
- Department of Pulmonology, Semmelweis University
- Thoracic Oncology Program

Ireland/United Kingdom
- Birmingham Group
- BTOG – British Thoracic Oncology Group
- ICORG – All Ireland Cooperative Oncology Research Group
- London Lung Cancer Group
- Manchester Lung Cancer Group
- National Cancer Research Institute – Lung Cancer Clinical Study Group

Israel
- Israel Lung Cancer Group
- Tel-Aviv Medical Center

Italy
- AIOT – Associazione Italiana di Oncologia Toracica
- GiMe – Italian group for the research and therapy of Mesothelioma
- Medical Oncology, Azienda Ospedaliera Universitaria Integrata
- National Cancer Institute, Pascale Foundation
- Perugia University Hospital Oncology Department

Netherlands
- NVALT – Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose
- ROTS - Rotterdam Thoracic Oncology Study Group

Norway
- NLCG – Norwegian Lung Cancer Group

Poland
- Polish Lung Cancer Group
- Medical University of Gdansk TOP Group

Portugal
- GECP – Grupo de estudos do cancro do pulmão
- Centro Hospitalar do Porto

Spain
- SLCG – Spanish Lung Cancer Group
- CIBERES – Biomedical Research Center on Respiratory Diseases

Sweden
- Swedish Lung Cancer Study Group

Switzerland
- SAKK – Schweizerische Arbeitsgemeinschaft fuer Klinische Krebsforschung

The Netherlands
- NVALT – Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose
- ROTS - Rotterdam Thoracic Oncology Study Group

United Kingdom/Ireland
- Birmingham Group
- BTOG – British Thoracic Oncology Group
- ICORG – All Ireland Cooperative Oncology Research Group
- London Lung Cancer Group
- Manchester Lung Cancer Group
- National Cancer Research Institute – Lung Cancer Clinical Study Group

Outside Europe:
- Australia – Princess Alexandra Hospital
- U.S.A. – Roswell Park Cancer Institute
- China – Shanghai Chest Hospital
ETOP as platform for information and meetings

- ETOP Slide decks – Highlights from ASCO, WCLC and ESMO Congresses
- 5th ETOP Residential Workshop: September 1-3, 2016 in Amsterdam, Netherlands
- ETOP Annual Meeting: November 11-12, 2016 in Amsterdam, Netherlands
ETOP clinical trials: Second or further line NSCLC

NSCLC without oncogenic driver mutation

- **EMPHASIS:** Phase III second line erlotinib versus docetaxel in advanced squamous NSCLC stratified by VeriStrat Good vs VeriStrat Poor (closed)

NSCLC with oncogenic driver mutation

- **NICHE:** Afatinib in HER2 mutated NSCLC: Phase II Simon two-stage design with disease control rate as primary endpoint methods (open)
- **BOOSTER:** Osimertinib with or without bevacizumab in T790M positive NSCLC with activating EGFR mutation (in preparation)
- Alectinib for RET driven tumors (in preparation)
NICHE: Afatinib for HER2 mutated NSCLC

Study design: Multicentre, open label, phase II trial, ETOP sponsored

Primary endpoint: Disease control (CR / PR / SD) lasting at least 12 weeks

Sample size: 22 patients

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<th>Screening, eligibility and enrolment</th>
<th>Trial treatment</th>
<th>Progression</th>
<th>Follow up</th>
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<tr>
<td>Stage IIB / IV NSCLC, pretreated</td>
<td>Afatinib 40mg daily p.o. until PD or unacceptable toxicity</td>
<td>CT week 20, then every 8 weeks until PD</td>
<td>For 6 months after enrollment of last patient</td>
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<tr>
<td>HER2 mutation confirmed locally</td>
<td>CT T&amp;A CT or MRI brain</td>
<td>CT week 6</td>
<td>......</td>
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<tr>
<td></td>
<td>CT week 12</td>
<td>CT week 12</td>
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ETOP clinical trials: First line therapy

NSCLC without oncogenic driver mutation:

• **SPLENDOUR**: Phase III study on first line chemotherapy in advanced NSCLC with or without denosumab stratified according to histology, bone involvement and region (EORTC, CECOG, and others) (open)

• **NICOLAS**: Feasibility of anti-PD1 nivolumab consolidation after standard first line chemoradiotherapy in locally advanced stage IIIA/B NSCLC (open, first amendment in preparation)

NSCLC with oncogenic driver mutation

• **BELIEF**: Phase II study on first line therapy in EGFR mutated NSCLC stratified according to T790M status as determined by sensitive methods (SLCG) (closed)
SPLENDOUR: A randomised, open-label phase III trial evaluating the addition of denosumab to standard first-line anticancer treatment in advanced NSCLC

Sample size: 1000

Primary endpoint: Overall survival

*ETOP | Group Presentation| TACT General Assembly | Chicago, June 3, 2016*
NICOLAS: A feasibility trial evaluating anti-PD1 nivolumab consolidation after standard first line chemotherapy and radiotherapy in locally advanced stage IIIA/B NSCLC

Screening, eligibility and enrolment

Stage IIIA / B NSCLC
Investigator’s choice

Whole body FDG PET-CT

Standard treatment

chemo cycle 1
chemo cycle 2
chemo cycle 3
Radiotherapy
66Gy, 33 fractions

Radiotherapy
66Gy, 24fractions

Trial treatment

Anti PD-1 consolidation:
nivolumab 10mg/kg every 2 weeks

Year 1: CT every 8 weeks
Year 2: CT every 12 weeks

Chemotherapy: Cisplatin (or Carboplatin) doublet

• PE: Grade ≥3 pneumonitis free rate; N = 43 pts
ETOP clinical trials: Resected NSCLC

Retrospective biomarker study stages I-III:

• Lungscape

Adjuvant study in stage IB-III:

• PEARLS: Adjuvant anti-PD1 antibody in resected NSCLC. Collaboration with EORTC, MSD is sponsor
Time to relapse according to pathological stage

- Peters, JTO in press

Events 5-Yr TTR
- IA: 129, 73.6%
- IB: 184, 68.8%
- IIA: 165, 58.0%
- IIB: 126, 53.4%
- IIIA: 325, 29.9%
- IIB: 26, 28.8%

Logrank Test: p-value <0.001

No at Risk
- IA: 560 515 462 409 275 172 94 45 24 7 1
- IB: 644 557 474 414 297 187 108 56 28 8 2
- IIA: 415 339 274 232 169 99 61 35 20 3 0
- IIB: 282 214 171 139 93 55 31 19 8 5 1
- IIIA: 499 309 210 154 97 51 24 11 8 2 1
- IIB: 39 18 11 10 6 2 0

- Peters, JTO 2014
PEARLS: Phase III trial of adjuvant pembrolizumab in stages IB-III NSCLC

Co-primary Endpoints:
- DFS in the PD-L1 strong positive sub-group;
- DFS in the overall population

Secondary endpoints:
- DFS in the PD-L1 positive population;
- OS in the PD-L1 strong positive subgroup
- OS in the overall population
- LCSS
ETOP clinical trials: Other histologies

Small cell lung cancer:

• **STIMULI:** Randomizes phase II study in limited disease SCLC treated with chemoradiotherapy with or without ipilimumab and nivolumab consolidation

Mesothelioma

• **PROMISE-meso:** Anti-PD1 antibody in malignant pleural mesothelioma (in preparation)

Thymic Carcinoma

• **Nivothym:** Anti-PD-1 in thymic carcinoma (EORTC collaboration)
STIMULI: SCLC LD amended protocol

- Study design: Multicentre, open label, randomized phase II trial, ETOP sponsored, collaboration with IFCT and other trial groups
- Primary objectives: PFS and OS
- Sample size: 260 randomized patients

**Chemo-Radiotherapy:**
cis-carboplatin + etoposide
4 cycles

**Biomaterial for translational research:**
Consolidation vs observation:
induction
maintenance
combination nivolumab/ipilimumab
nivolumab

**Screening:**
LD SCLC

**Tumour evaluation:**
PD no
PD yes
off

**Chemo-Radiotherapy:**
cis-carboplatin + etoposide
4 cycles

**Consolidation vs observation:**
induction
maintenance
combination nivolumab/ipilimumab
nivolumab

**RT (Thoracic Radiotherapy):**
accelerated schedule preferred
start: day 1 of chemo cycle 1 or day 1 of chemo cycle 2

**CT scans for tumour assessment**
- up to 18 months: every 9 weeks
- up to 2 years: every 12 weeks
- years 3 & 4: every 6 months
- at 5 years

**At progression:**
Voluntary re-biopsy: → FFPE block

**Biomaterial for translational research:**
Serum
Whole blood
Biopsy: FFPE block or slides
Thank you for listening!