Ongoing Early Clinical Trials, France May 2019

Phase 1:

- **Leukemia:**
  - ITCC-052 Carfilzomib + R3 to reopen
  - ITCC-054 Bosutinib
  - ITCC-059 Inotuzumab Ozogamycin
  - Quizartinib
  - Zuma 4

- **Solid:**
  - Eribulin-mesilate/ /E7389-G000-213
  - Talimogene Laherparepvec
  - ITCC-037 Dabrafenib (BRAFv600) (Phase 2)
  - ITCC-047 Regorafenib + VI
  - Trametinib (MEK) (Phase 2)
  - ITCC-050, Lenvatinib (Phase 2)
  - ITCC-049 Afatinib (Expansion)
  - Pembrolizumab (PD-1L positive) (Phase 2)
  - ITCC-061 EPZ 6438 Tamezetostat (Closed to inclusion on dec 18. Reopening on march 2019?)
  - ITCC-055 Cobimetinib
  - ITCC-057 AcSe-ESMART A-C-D, I
  - ITCC-065 Ibrutinib + Rice
  - ITCC-066 LOXO-101
  - LOXO-195
  - Venetoclax

Phase 2:

- **Leukemia/Lymphoma:**
  - Nivolumab-brentuximab CA209744 Daratumumab - Protocol 54767414ALL2005
  - Nivo-ALCL

- **Multiple:**
  - Metro PD1(ph 1-2)
  - Tamezetostat: Rhaboid and INI-neg >16 yr
  - Pazopanib GW786034

- **Sarcoma:**
  - Regobone: Ewing > 10yrs
  - Pembrosarc >18yrs
  - Metzolimos

- **Brain Tumors:**
  - ITCC-022 VINILO Ph2 Randomization
  - ITCC-051 BIOMEDE
  - ITCC-064 ABT-414 >12yrs
  - CRDB436G2201:Dabrafenib –Trametinib:

- **Molecular Profiling:**
  - MAPPYACTS

> 18 years one may also consider adult phase I/II trials in adult centers
Leukemia
Phase I
Phase 1b/2 Study of Carfilzomib in combination with Dexamethasone, Mitoxantrone, PEG-asparaginase, and Vincristine (R3 Induction Backbone) in pediatric subjects with relapsed or refractory Acute Lymphoblastic Leukemia

**CFZ008 / ITCC-052 / NCT02303821**

- Carfilzomib (Kyprolis®) = proteasome inhibitor, irreversible, less neurotoxic than bortezomib
- Relapsed (Phase1b and 2) or refractory ALL (Phase1b only) with ≥5% blasts in bone marrow (M2 or M3 disease), +/- extramedullary disease
- < 18 years
- Reopen with new back bone VXLD without lead-in-window

- Sponsor: Onyx/Amgen; PI: A Baruchel
- Centers F/contacts:
  - R Debré: A Baruchel - CHRU de Lille: B Nelken
  - Trousseau: G Leverger
  - Bordeaux: S Ducassou
  - Nancy: C Schmitt
  - Toulouse: M Pasquet
Study Evaluating the Safety and Efficacy of Eribulin Mesilate in Combination With Irinotecan Hydrochloride in Children With Refractory or Recurrent Solid Tumors /E7389-G000-213/ NCT03245450

Inclusion criteria:
• Phase 1: Relapsed/refractory solid tumors (excluding CNS tumors)
• Phase 2: relapsed/refractory RMS, NRSTS, EWS
• Age: > 6 months and < 18 years old

Primary endpoint:
• Phase 1: DLT, MTD
• Phase 2: ORR

Sponsor: Eisai Inc.
PI:?

Centers:
Curie: Dr I Aerts(Not open actually)
COL:
Ihope: Dr Corradini
Marseille:
A phase I/II study of Bosutinib in pediatric patients with Chronic Myeloid Leukemia who are resistant or intolerant to at least one prior Tyrosine Kinase Inhibitor therapy

**ITCC-054**

- Bosutinib = 3\textsuperscript{rd} generation BCR/ABL inhibitor
- CML resistant (subopt response or failure) or intolerance to at least one prior tyrosine kinase inhibitor
- \(\geq 1\) month - \(< 18\) years

- Sponsor: Pfizer, PI: M Zwaan
- Centers F/contacts: PI: B Brethon
- Nantes?\+/\-Lyon?
T2015-001 A phase I study of Inotuzumab Ozogamycin as a single agent and in combination with chemotherapy for pediatric CD22-positive relapsed/refractory Acute Lymphoblastic Leukemia

ITCC-059

• Inotuzumab Ozogamycin = anti-CD22 monoclonal antibody
• 1 month - ≤ 18 years

Sponsor: Erasmus Rotterdam, PI: M Zwaan
• Centers F/contacts: PI: A Baruchel
  – Robert Debré
  – CHRU de Lille :Dr B Nelken
A Phase 1/2, Multicenter, Dose-Escalating Study To Evaluate the Safety, Pharmacokinetics, Pharmacodynamics, and Efficacy Of Quizartinib Administered in Combination With Re-Induction Chemotherapy, and as a Single-Agent Maintenance Therapy, in Pediatric Relapsed/Refractory AML Subjects Aged 1 Month to <18 Years (and Young Adults Aged up to 21 Years) With FLT3-ITD Mutations (https://clinicaltrials.gov/ct2/show/NCT03793478)

• **Inclusion criteria:**
  • FLT3-ITD positive AML, > 1 month and < 21 years of age
  • First relapse or refractory to first-line high-dose chemotherapy with no more than 1 attempt (1–2 cycles of induction chemotherapy) at remission induction - prior HSCT is permitted

• **Primary endpoint:**
  • Composite complete remission (CRc) rate

• **Sponsor:** Daiichi Sankyo, Inc.
• **PI:**
• **Centers:** Belgium, Denmark, France, Israel, Netherlands, Spain
• **Centers in France:** 3
  • IHOPE: Pr BERTRAND
  • CHRU de Toulouse: Dr Pasquet
  • Armand Trousseau: Dr Petit
A Phase 1/2 Multi-Center Study Evaluating the Safety and Efficacy of KTE-C19 in Pediatric and Adolescent Subjects With Relapsed/Refractory B-precursor Acute Lymphoblastic Leukemia (ZUMA-4)

- Primary Outcome Measures :
  - Phase 1: Percentage of Participants Experiencing Adverse Events Defined as Dose-Limiting Toxicities (DLT)
  - Phase 2: Overall Complete Remission Rate

- Secondary Outcome Measures :
  - Duration of Remission
  - Minimum Residual Disease Negative Remission Rate
  - Allogeneic Stem Cell Transplant Rate
  - Overall Survival
  - Relapse-Free Survival

- Sponsor: Kite, A Gilead Company
- PI:
- Centers:
  - RDB: Pr A Baruchel
  - Ihope: Pr Y Bertrand
  - APHM: Pr G Michel
Phase II
Risk-based, response-adapted, Phase II open-label trial of nivolumab + brentuximab vedotin for children, adolescents, and young adults with relapsed/refractory CD30 + Hodgkin lymphoma after failure of first-line therapy, followed by brentuximab + bendamustine for participants with a suboptimal response.

CA209744 - NCT02927769

- Hodgkin lymphoma: only first relapse
- Age: 5 - 30 years
- Exclusion: previous allogeneic and/or ASCT, immune check-point
- Cohort R1: low risk
- Cohort R2: standard risk
- Nivo + Brentuximab 4 Cycles, then PET/CT (central review)
  ⇒ if CR: RT (R1) or ASCT (R2)
  ⇒ If PR: Bv + Bendamustine 2 cycles; > if CR: RT (R1) or ASCT (R2)

- Sponsor: BMS
- Centers:
  - Lille: A Lamblilliotte
  - Nancy: C Schmitt
  - Robert Debré: T Leblanc
  - Lyon: N Garnier
  - Trouseau: J Landman-Parker
  - Gustave Roussy: S Abbou
  - Marseille: G Michel
  - Toulouse: G Plat
Phase I
Phase II trial of nivolumab for pediatric and adult relapsing/refractory ALK+ anaplastic large cell lymphoma, for evaluation of response in patients with progressive disease (Cohort 1) or as consolidative immunotherapy in patients in complete remission after relapse (Cohort 2) / NCT03703050

- Cohort 1: estimate the efficacy of nivolumab treatment in patients with relapsed/refractory ALK+ ALCL in terms of best objective response within the first 24 weeks
- Cohort 2: estimate the efficacy of nivolumab treatment as consolidative immunotherapy after CR in patients with relapsed/refractory ALK+ ALCL in terms of progression-free survival

- Sponsor: IGR
- PI: Dr Laurence Brugières
- Centers:
  - IGR: Dr V Minard
  - Ihope: Dr MICHALLET
  - Nancy: Dr Contet
  - Toulouse:
  - Bordeaux: S Ducassou
An Open-label, Multicenter, Phase 2 Study Evaluating the Efficacy and Safety of Daratumumab in Pediatric and Young Adult Subjects ≥1 and ≤30 Years of Age With Relapsed/Refractory Precursor B-cell or T-cell Acute Lymphoblastic Leukemia or Lymphoblastic Lymphoma Protocol 54767414ALL2005

Primary Objective
• To evaluate the efficacy of daratumumab in addition to standard chemotherapy as measured by the CR rate.

Secondary Objectives
• To assess the efficacy of daratumumab in addition to standard chemotherapy, including
• ORR, RFS, EFS, and OS and minimal residual disease (MRD) negative rate in subjects with B-cell and T-cell ALL
• To assess the safety and tolerability of daratumumab in addition to standard chemotherapy in pediatric and young adult subjects with B-cell and T-cell ALL…

Sponsor: Janssen Research & Development, LLC
• PI: Pr. A. BARUCHEL
Center:
• Robert Debré: Dr A Baruchel
• Trousseau: Dr A Petit
• Nancy: Dr Contet
• Bordeaux: Dr Ducassou
• Ihope: Pr Y Bertrand
Solid tumors
A Phase 1, Multi-center, Open-label, Dose De-escalation Study to Evaluate the Safety and Efficacy of Talimogene Laherparepvec in Pediatric Subjects With Advanced Non-central Nervous System Tumors that are Amenable to Direct Injection.\textit{NCT02756845}

- Talimogene Laherparepvec
- Cohort A1 (12 to ≤ 21 years of age)
- Cohort B1 (2 to < 12 years of age)
- Sponsor: Amgen
- PI France: Dr Bergeron

Centers:
- Lyon: Dr P Leblond
- Marseille: Dr André
- Curie: Dr Aerts Isabelle
Phase I/IIa, 2-Part, Multi-Center, Single-Arm, Open-Label Study to Determine the Safety, Tolerability and Pharmacokinetics of Oral DABRAFENIB in Pediatric Subjects Aged 1 Month to <18 Years with Advanced BRAF V600-Mutation Positive Solid Tumors

ITCC-037/ NCT01677741

- Dabrafenib = oral inhibitor of BRAF V600
- **Relapsed or refractory solid tumors with BRAFv600 mutations**
- > 1 mo – < 18 years
- Part 2:
  - **Cohort A**: low-grade gliomas with BRAF V600 mutations (closed)
  - Cohort B: high-grade gliomas with BRAF V600 mutations
  - Cohort C: LCH with BRAF V600 mutations
  - Cohort D: other tumors that have BRAF V600 mutations (e.g., PTC, melanoma)

- **Sponsor**: GSK/Novartis; PI: B Geoerger
- **Centers/contact**: EU + US
  - IGR: B Geoerger - Marseille: A Verschuur
  - Institut Curie: I Aerts - Toulouse: Al Bertozzi
  - Trousseau: J Donadieu
An Open-Label, Dose-Escalation, Phase I/II Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics and Clinical Activity of the MEK Inhibitor **TRAMETINIB** in Children and Adolescents Subjects with Cancer or Plexiform Neurofibromas and Trametinib in **Combination with Dabrafenib** in Children and Adolescents with Cancers Harboring V600 mutations

**GSK1120212 / NCT02124772**

- Trametinib = oral MEK inhibitor
- **Relapsed or refractory tumors**
- ≥ 1 months and ≤ 18 years
- **Part A: Dose-escalation: reopened:** < 6 years
- **Part B:**
  1. Neuroblastoma
  2. LGG with BRAF tandem duplication (*closed*)
  3. NF1 with PN (*closed*)
  4. BRAFv600 mutations or other markers of MAPK pathway activation
- **Part C:** Trametinib + Dabrafenib in BRAFv600 mutated tumors (3+3 escalation)
- **Part D:** Trametinib + Dabrafenib in BRAFv600 mutated LGG + LCH
- PK, PD, Biology
- Tox: Skin, fatigue, vision disorder, nausea, vomiting, QTc prolongation

- Sponsor: GSK/Novartis; PI: I Aerts
- Centers F/Contacts:
  - Institut Curie: I Aerts
  - Gustave Roussy: B Geoerger
A PHASE I/II, MULTICENTER, OPEN-LABEL, DOSE-ESCALATION STUDY OF THE SAFETY AND PHARMACOKINETICS OF COBIMETINIB IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH PREVIOUSLY TREATED SOLID TUMORS

GO29665 / ITCC-055/ NCT02639546

- Cobimetinib = oral MEK inhibitor
- **Relapsed or refractory tumors**
- ≥ 6 months to < 18 years (in expansion: to < 30 years)
- Diseases with RAS pathway activation
- Dose-escalation: *ongoing*
- Expansion: according to signals
- PK, PD, Biology
- Tox: Skin, fatigue, vision disorder, nausea, vomiting, QTc prolongation

- Sponsor: Roche; PI: B Geoerger
- Centers F/Contacts:
  - Gustave Roussy: B Geoerger
  - Institut Curie: J Michon
  - La Timone: A Verschuur
  - Trousseau: Landmann/Petit
A Study of **PEMBROLIZUMAB** (MK-3475) in Pediatric Participants With Advanced Melanoma or Advanced, Relapsed, or Refractory PD-L1-Positive Solid Tumors or Lymphoma - KEYNOTE-051/ NCT02332668

- Pembrolizumab = anti PD1 antibody
- **PD-L1 positive solid tumors, melanoma CNS except DIPG**
  - Pre-screening mandatory at MSD: PD-L1 IHC (not needed for Melanoma)
- 6 months to 17 years
- **Phase 1: dose validation (closed)**
- Phase 2: now only (dec 2018): melanoma, MSI-high, HD
- Measurable disease
- IV q 3 weeks

- Sponsor: MSD;
- Centers/contacts: 1 in F, + 1 UK, USA, Israel
  - Gustave Roussy: B Geoerger
A Phase 1, multi-center, open-label, non-randomized, dose escalation design study of **REGORAFENIB** (BAY 73-4506) in paediatric patients from 6 months to less than 18 years with a solid malignant tumour refractory to standard therapy.  **ITCC-047/ NCT02085148**

- Regorafenib = muti-targeting agent (RET, VEGFR1, VEGFR2, VEGFR3, KIT, PDGFR-alpha, PDGFR-beta, FGFR1, FGFR2, TIE2, DDR2, TrkA, Eph2A, RAF-1, BRAF, BRAFV600E , SAPK2, PTK5, and Abl)
- **Recurrent or refractory solid tumors**
- 1 yrs - ≤ 18 years
- Regorafenib oral in 2 schedules
- VCR-irinotecan

- Sponsor: Bayer; PI: B. Geoerger
- Centers/contacts: 5 centers in F + UK
  - IGR: B Geoerger
  - I Curie: I Aerts
  - IHOPE: D Frappaz
Phase I/IIa, Study of LENVATINIB in Children and Adolescents With Refractory or Relapsed Solid Malignancies
E7080-G00-207/ITCC-050 / NCT02432274

- Lenvatinib = muti-targeting agent (RET, VEGFR1, VEGFR2, VEGFR3, KIT, PDGFR-alpha, FGFR1, FGFR2, FGFR3, FGFR4)
- Relapsed or refractory solid tumors, including CNS
- > 2 years – < 18 years
- Cohort 1: Dose Escalation in solid tumors (closed)
- Cohort 2:
  - Cohort A: ^131^iodine-refractory differentiated thyroid cancer (DTC)
  - Cohort B: osteosarcoma <25 years
- Cohort 3:
  - Cohort A: Dose escalation in combination with IFO and VP16 in osteosarcoma <25 years
  - Cohort B: expansion
- Sponsor: EISAI; PI: N Gaspar
- Centers/contact: EU + US
  - Gustave Roussy: N Gaspar
  - Institut Curie: I Aerts
  - Strasbourg: N Entz Werlé
  - Nantes: S Dumoucel
  - Toulouse: M Gambart
  - I hope: N Corradini
Phase I open label, dose escalation trial to determine the MTD, safety, PK and efficacy of **AFATINIB** monotherapy in with known ErbB pathway deregulation regardless of tumour histology

**ITCC-049/ NCT02372006**

- Afatinib = oral irreversible pan-ERB inhibitor (EGFR, HER2, ErbB3 and ErbB4)
- **Solid tumors possibly ErbB-driven, Neuroectodermal tumors, RMS, others**
- 2 years to<18 years
- Dose finding (**closed**);
- Expansion: pre-screening EGFR or HER2 IHC and FISH
- Tox: skin, diarrhea, pulmonitis, nail abnormalities

- Sponsor: Boehringer Ingelheim, PI: B. Geoerger
- Centers/contact (in France):
  - Gustave Roussy: B Geoerger
  - Institut Curie: I Aerts
  - COL: P Leblond
  - Toulouse: M Gambart
  - IHOPE Lyon: D Frappaz
  - Bordeaux: S Ducassou
A Phase 1 Study of the EZH2 Inhibitor Tazemetostat in Pediatric Subjects With Relapsed or Refractory INI1-Negative Tumors or Synovial Sarcoma

NCT02601937 / ITCC-061

- TAZEMETOSTAT = oral EZH2 inhibitor (oral solution)
- Closed to inclusion on dec 2018. Reopening on March 2019?
- ≥ 6 mo to ≤ 21 years
- Phase I: relapsed or refractory evaluable INI-neg
  - Rhabdoid tumors: MRT, ATRT, RTK
  - INI1 negative tumors: Epithelioid sarcoma, Epithelioid MPNST, Extraskeletal myxoid chondrosarcoma, Myoepithelial carcinoma, Renal medullary carcinoma etc.
  - Synovial sarcoma (SS18-SSX rearrangement)
- Expansion: measurable INI-neg rhabdoid tumors (MRT, ATRT, RTK)

- Sponsor: EPIZYME; PI: F Bourdeaut
- Centers/contact/France:
  - Institut Curie: F Bourdeaut
  - Gustave Roussy: B Geoerger
European Proof-of-Concept Therapeutic Stratification Trial of Molecular Anomalies in Relapsed or Refractory Tumor

ITCC-057/ NCT02813135

- Relapsed, refractory malignancies, effective standard therapy
- < 18 years (≥18 if pediatric disease)
- Molecular profiling (WES, RNAseq) done
- Evaluable or measurable disease
- Neutros: >1000; Platelets: >100 000

- Sponsor: Gustave Roussy, PI: B Geoerger
- Centers/contact:
  - Gustave Roussy: B Geoerger
  - I Curie: I Aerts
  - IHOPE: N Corradini
  - CHU Nantes: E Thebaud
  - CHRU Bordeaux: S Ducassou
  - Trouseau: J Landman-Parker
  - COL: P Leblond
  - Marseille: A Verschuur
  - CHU Angers: E Di Carli
Arm A: Ribociclib + Topotecan and Temozolomide
Arm B: Ribociclib + Everolimus (closed)

- Ribociclib (LEE011) = oral CDK4/6 inhibitor &
  A. Topotecan iv – temozolomide oral D1-5
  B. Everolimus = oral mTOR inhibitor (closed)
- ctDNA, PD, PK (arm B)

- Enrichment:
  A. CDK4/6 pathway activated tumors with wild-type Rb gene; TOTEM of interest
  B. CDK4/6 pathway activated tumors with wild-type Rb gene; PI3K/AKT/mTOR path & MYCN anomalies
Arm C: AZD1775 + Carboplatin
Arm D: Olaparib + Irinotecan

C. AZD1775 = Wee1 inhibitor PO BID &
   - Carboplatine, IV every 21 Days
D. Olaparib = PARP inhibitor PO BID &
   - Irinotecan IV 5 days
• ctDNA, PK, PD

• Enrichment:
C. DSB repair deficiency; TP53, MYCN, RAS activating mut/amp; carboplatin of interest
D. DSB repair deficiency; Ewing sarcoma with EWS/FLI or EWS/ERG translocation; irinotecan of interest

• Able to swallow capsules
Arm I: Enasidenib

- Enasidenib = oral IDH2 inhibitor
- **Specific Arm “eligibility/selection” criteria**
  1. Patient must have documented IDH2 gene-mutated disease and had at least 2 prior induction therapy
  2. Patient with IDH2 germline mutations and significant clinical deficit of the disease will be allowed
  3. For patients with documented IDH2 mutation eligible for this treatment arm, the inclusion criteria of extensive molecular profiling of the recurrent tumor may be waved

- **100 % equivalent of the adult RP2D/ 100% enrichment**

- Enasidenib orally on a continuous dosing once daily (QD) per 28 day cycle

- **Open**
- **Able to swallow capsules**
Ibrutinib randomized safety and efficacy study in pediatric patients with mature B-cell NHL, including Burkitt lymphoma/Leukemia and Diffuse Large B-cell Lymphoma
54179060LYM3003 / ITCC-065/ NCT02703272

- Ibrutinib = oral Bruton kinase inhibitor
- Mature B-cell NHL, recurrent or primarily refractory
- Part 1: Ibrutinib orally plus RICE or RVICI
- Part 2: Randomization 2:1 RICE or RVICI +/- Ibrutinib
- 1 year to < 18 years
- Measurable disease

- Sponsor: Janssen
- F Centres /contacts: PI: V Minard-Colin
  - Gustave Roussy: V Minard-Colin - Marseille: A Verschuur
  - CHU Lille: B Nelken - Bordeaux: N Aladjidi
  - IHOPE: Dr Garnier - Toulouse: Dr Plat
  - Nancy (Vandoeuvre): Dr Phulpin - Nantes: Dr Couëc
A Phase 1/2 Study of the Oral TRK Inhibitor LOXO-101 in Pediatric Patients with Advanced Solid or Primary Central Nervous System Tumors / ITCC-066 / NCT02637687

- LOXO-101 = oral NTRK inhibitor
- Cancer with fusion involving NTRK1, NTRK2, or NTRK3
- ≥ 1 month to 21 years
- Evaluable disease
- PK, PD, ctDNA, QoL

- Sponsor: Loxo Oncology
- F Centres /contacts: PI: F Doz
  - I Curie: F Doz
  - Gustave Roussy: B Geoerger
Phase 1/2 Study of LOXO-195 in Patients With Previously Treated NTRK Fusion Cancers/ NCT03215511

- LOXO-195 = oral NTRK inhibitor developed against LOXo-101 resistances
- Cancer with fusion involving NTRK1, NTRK2, or NTRK3 that are refractory/relapse after LOXO-101
- ≥ 1 month
- Evaluable disease and/or measurable disease

- Sponsor: Loxo Oncology
- F Centres /contacts: PI: B. Besse
  - Gustave Roussy: B Geoerger
  - I Curie: Pr F Doz
A Phase 1 Study of the Safety and Pharmacokinetics of Venetoclax in Pediatric and Young Adult Patients With Relapsed or Refractory Malignancies M13-833 VENETOCLAX/ NCT03236857

Inclusion criteria:
Relapse/refractory tumors (CNS tumors excluded)
Age: < 25 years old

Primary Outcome Measures:
Recommended Phase 2 dose (RPTD) o
Number of Participants with Dose limiting toxicities (DLT) of Venetoclax Monotherapy

Secondary Outcome Measures:
Objective Response Rate (ORR)
Partial Response (PR)
Complete Response (CR) rate

Sponsor: AbbVie/Roche-Genentech
PI: Pr A Baruchel
Centers:
I Curie: I Aerts
Ihope: Dr N Corradini
Marseille: Dr A Veerschuur
RDB: Pr A Baruchel
Trouseau: Pr Petit
Toulouse: Dr Gambart
Phase II
Nivolumab in Combination With Metronomic Chemotherapy in Paediatrics Refractory / Relapsing Solid Tumors or Lymphoma / Etude de phase 1-2/ NCT03585465

- **Inclusion criteria:**
  - Solid malignant tumor, or lymphoma
  - Age: > 4 and < 18 years old

- **Primary endpoint:**
  - DLT, PFS

- **Sponsor:** Centre Oscar Lambret.

- **PI:** Dr P Leblond

- **Centers:**
  - CENTRE OSCAR LAMBRET: Dr Hélène SUDOURLBONNANGE
  - HÔPITAL LA TIMONE ENFANTS: Dr Nicolas ANDRE
  - NANTES: ??
  - STRASBOURG: Dr Natacha ENTZ-WERLE
  - IHOPE : Dr Nadège CORRADINI
  - Toulouse: Dr Marion Gambart
  - INSTITUT CURIE : Dr Isabelle AERTS
Phase I-II Study of Vinblastine in Combination with Nilotinib in Children and Adolescents with Refractory or Recurrent Low-Grade Glioma: A SIOPE-Brain Tumor and ITCC protocol

ITCC-022 VINILO/ NCT01887522

- Vinblastin iv weekly + Nilotinib orally daily
- **Relapsed or refractory LGG**
- > 6 mo – < 21 years
- **Phase 1:** dose escalation closed
- **Phase 2:** randomized VBL vs VBL + Nilotinib
- Toxicity: toxidermia, neutropenia, PRES, rash, fatigue, weight loss, liver enzyme increase

- **Sponsor:** Gustave Roussy; PI: J Grill
- **Centers:**
  - IGR: J Grill
  - I Curie: F Doz
  - Toulouse: Al Bertozzi
  - Marseille: N Andre
  - Bordeaux: C Icher
  - Saint-priest-en-jarez: - Angers: E de Carli
  - Nancy: P Chastagner
  - Poitiers: F Millot
  - Tours: M Yvert
  - St Etienne: C Berger
  - Grenoble: A Pagnier
  - Strasbourg: N Entz-Werle
  - I Hope: D Frappaz
A Phase II Study of **Pazopanib GW786034**, NSC# 737754 in Children, Adolescents and Young Adults With Refractory Solid Tumors

- **Pazopanib**
- Young Adults With Refractory Solid Tumors:
  - RMS, nbl, hepatoblastoma: cohorts opened
  - NON RMS, ewing sarcoma, peripheral pnet: enrollment on hold
- 1 Year to 18 Years
- Sponsor: Novartis
- PI France: Isabelle Aerts
- F Centres /contacts:
  - Institut Curie: I Aerts
Biological Medicine for Diffuse Intrinsic Pontine Glioma (DIPG) Eradication: BIOMEDE
ITCC-051 BIOMEDE/NCT02233049

- **Newly diagnosed pontine glioma**
- Biopsy at diagnosis: PTEN loss, EGFR ampli
- >6 mo - < 25 years
- Stratification and Randomization according to FISH:
  - R1: erlotinib versus dasatinib
  - R2: everolimus versus dasatinib
  - R3: erlotinib versus everolimus versus dasatinib

- **Sponsor**: Gustave Roussy; PI: J Grill
- **Centers/contacts**:
  - IGR: J Grill
  - I Curie: F Bourdeaut
  - CLB: C Faure Conter
  - Marseille: N Andre
  - Rennes: C Chape
  - Amiens: C Devoldere
  - Besancon: V Laithier
  - Dijon: G Couillault
  - COL: P Leblond
  - Angers: E de Carli
  - Toulouse: Al Bertozzi
  - Nancy: P Chastagner
  - Bordeaux: C Icher
  - Brest: P Le Moine
  - Clermont Ferrand: J Kanold
  - Grenoble: A Pagnier
  - Rouen: JP Vannier
  - Poitiers: F Millot
  - Reims: S Gorde-Grosjean
  - Strasbourg: N Entz-Werle
  - Tours: M Yvert
  - St Etienne: C Berger
  - Nice: C Soler
  - Montpellier: G Palenzula
Etude Internationale multicentrique de phase 2 randomisée qui évalue et compare 2 stratégies de traitement pour les patients atteints de neuroblastome métastatique avec une réponse insuffisante à la chimiothérapie d’induction/ Etude Veritas/NCT03165292

- Objectif principal: efficacité de 2 stratégies d’intensification chez les patients à très haut risque en terme de survie sans événement depuis la date de randomisation.
- Critères d’inclusion:
  1. Neuroblastome métastatique
  2. Patient traité par le protocole HRNBL SIOPEN en cours ou traité avec le traitement standard actuel pour les neuroblastomes à très haut risque en dehors d’un essai
  3. Scintigraphie au mIBG positive au diagnostic et après la chimiothérapie d’induction (évaluation pre BuMel)
  4. Réponse métastatique après la chimiothérapie d’induction inférieure à une réponse partielle ou score SIOPEN > 3

- PI France: Dr Dominique Valteau Couanet
- Centres: 26 centres SFCE, dont 8 centres pour la phase d’intensification ; et 4 centres pour l’administration du MIBG thérapeutique
Combination of MK3475 and Metronomic Cyclophosphamide in Patients With Advanced Sarcomas : Multicentre Phase II Trial

PEMBROSARC - NCT02406781

- **Advanced leiomyosarcoma, undifferentiated sarcoma, other sarcoma, osteosarcoma, GIST (Ewing closed)**
- Age > 18 years (amendment >10 yrs planned)
- Pembrolizumab + Metronomic cyclo

- Sponsor: Institut Bergonié
- Centers:
  - Institut Bergonié
  - Centre Oscar Lambret
  - Centre Léon Bérard Institut
  - Paoli Calmettes Institut
  - Curie Institut de Cancérologie de l'Ouest
  - Institut Claudius Regaud
  - Gustave Roussy
A Randomized Phase II, placebo-controlled, multicenter study evaluating efficacy and safety of **REGORAFENIB** in patients with metastatic bone sarcomas

**REGOBONE/ NCT02389244**

- **Metastatic bone sarcoma**
- \( \geq 10 \) years
- Double-blind placebo-controlled trial, 3 strata:
  - Strata A: Osteosarcoma (Closed)
  - Strata B: Ewing sarcoma
  - Strata C: Chondrosarcoma

- **Sponsor:** Unicancer; PI: F Duffaud (La Timone)
- **Centers/contact:**
  - Marseille: F Duffaud
  - IGR: S Dumont
  - I Curie: S Piperno-Neumann
  - Lyon: JY Blay
  - Toulouse: C Chevreau
  - Nantes: E. Bompas
  - Lille: P Nicolas
A MULTICENTRIC PHASE IB TRIAL
MetZolimOS / EudraCT 2014-000196-85

- Metronomic Cyclophosphamide + Methotrexate + zoledronic acid + Sirolimus
- Pre-treated solid tumors with bone metastasis
- Expansion cohort: metastatic, locally advanced Osteosarcoma
- ≥ 13 years

- Sponsor: Institut Bergonie Bordeaux; PI: M Toulemonde
- Centers/contact:
  - IGR: S Dumont - I Bergonie, Bordeaux: M Toulemonde
  - Lille: P Nicolas - CLB Lyon: JY Blay
Phase II, Multicenter Study of the EZH2 Inhibitor **Tazemetostat** in Adult Subjects With INI1-Negative Tumors or Relapsed/Refractory Synovial Sarcoma

**NCT02601950**

- **TAZEMETOSTAT** = oral EZH2 inhibitor (tablets)
- Closed to inclusions on dec 2018. Reopening on march 2019?
- Relapsed or refractory tumors
- Measurable disease based on RECIST 1.1 or RANO (CNS tumors)
- > 16 years
- Phase II:
  - Cohort 1: rhabdoid tumors
  - Cohort 2: relapsed/refractory synovial sarcoma
  - Cohort 3 to 5: INI1-negative/aberrant tumor

- Sponsor: EPIZYME
- Centers/contact France:
  - Gustave Roussy: O Mir
  - Institut Curie: V Laurence
  - Bergonie: Bordeaux: A Italiano
  - CLB Lyon: YJ Blay
ABT-414 alone or ABT-414 plus Temozolomide vs. Lomustine or Temozolomide for Recurrent Glioblastoma (INTELLANCE 2)  
NCT02343406 / EORTC / ITCC-064

- ABT-414 = anti-EGFR monoclonal antibody drug conjugate (Auristatine)
- Recurrent glioblastoma
- > 18 years: Randomization
  - Arm 1: ABT-414 + Temozolomide
  - Arm 2: ABT-414 monotherapy
  - Arm 3A: ABT-414 + Lomustine: relapsing during TMZ treatment, or within 16+ weeks after last cycle
  - Arm 3B: ABT-414 + Temozolomide: re-challenge if relapse 16+ weeks after the last TMZ cycle

- Pediatric pats (0-18): ABT-414 (+TMZ at the investigator’s discretion)
  - HGG or DIPG
  - EGFR amplification or EGFRvIII

- Sponsor: EORTC (ABBVIE supported)
- Centers/contact:
  - Angers - Bobigny - Bron - Lille - Lyon: D Frappaz
  - Marseille - Nice - Paris - Saint Herbelin - Villejuif: S Dumont
Phase II Open-label Global Study to Evaluate the Effect of Dabrafenib in Combination With Trametinib in Children and Adolescent Patients With BRAF V600 Mutation Positive Low Grade Glioma (LGG) or Relapsed or Refractory High Grade Glioma (HGG) (NCT02684058)

- Trametinib + Dabrafenib
- **Relapsed or refractory tumors**
- ≥ 12 months and < 18 years
- **HGG cohort:** relapsed/progressive HGG
- **LGG cohort:** newly diagnosed patients. Randomization with VCR/Carboplatin

Sponsor: Novartis
PI France: Nicolas André
Center:
Lille:
Lyon:Dr D Frappaz
Marseille: Dr N André
Strasbourg:Dr Entz Werlé
Toulouse:
Curie:
Gustave Roussy
Molecular Profiling
MAPPYACTS  A multicentric, prospective proof-of-concept study
MoleculAr Profiling for Pediatric and Young Adult Cancer Treatment Stratification  NCT02613962 / ITCC-056

- Recurrent/refractory malignancy and eligible for early clinical trial
- WES and RNAseq
- Cf DNA, immune contexture
- Preclinical models and patient-derived xenografts
- ≥ 6 months

- Sponsor: Gustave Roussy; PI: B Geoerger
- Centers/contacts:
  - IGR: B Geoerger
  - I Curie: G Schleiermacher
  - IHOPE: D Frappaz, Y Bertrand
  - Marseille: N Andre
  - Nancy: P Chastagner
  - Trousseau: J Landman-Parker
  - Angers: E De Carli
  - Oscar Lambret Lille: P Leblond
  - Nantes: E Thebaud
  - Toulouse: M Gambart
  - Robert Debre: A Baruchel
  - Bordeaux: S Ducassou
  - Strasbourg: N Entz-Werle