RARE TUMOURS Committee
Thursday, June 2, 2016, 2:00pm – 4:00pm
State II Room, DoubleTree Hotel, Chicago

Chair: I.Ray-Coquard Co-Chair: J.Ledermann
Harmonization liaisons: Votan/Farelly (Ops), BH Nam/Paul (Stats)

- **Call to Order and Welcome**
  - COI declarations
  - Approval of Minutes/Report November 2015 (posted on GCIG website)
- **On-going clinical trials:**
  - Update on Alienor trial
- **New/Concepts proposals:**
  - New project on first line CCCov (report of the survey) M McCormack & data from JGOG (Aikou Akamoto)
  - New project for germ cell tumors (new version) KGOG JY Park
  - Registry for SCC, first inclusion Ray-Coquard
- **OTHER TOPICS**
  - Example of successful stories from other cancers/groups with JY Blay from WSN&EORTC for sarcoma experience & ERN (EU project of rare cancer network)
- **Discussion/Future Directions**
- **Adjourn**

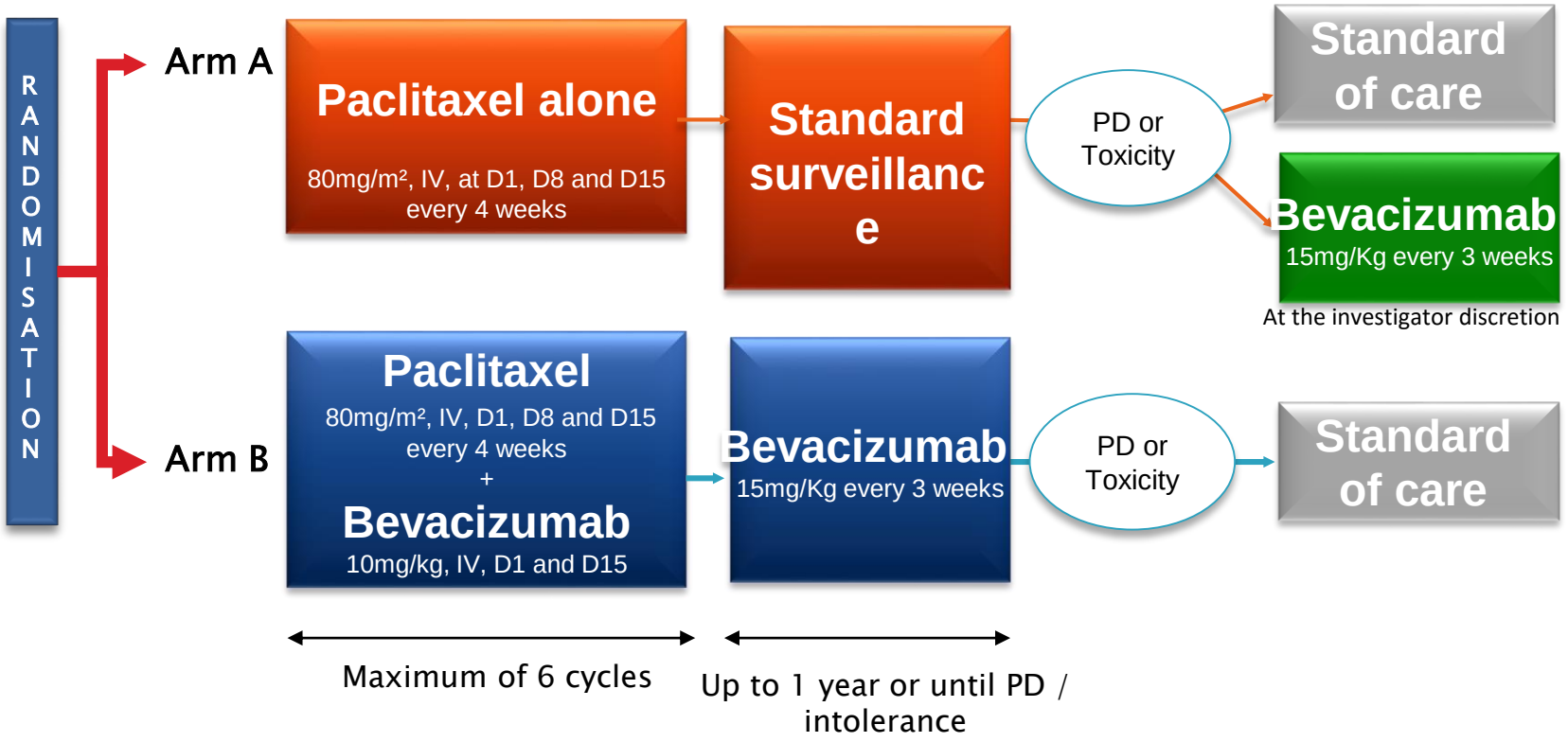
ALIENOR

ENGOT- OV7

Avastin and weekly pac**LI**taxel use in s**E**x cord-stromal ovaria**N** tum**OR**s

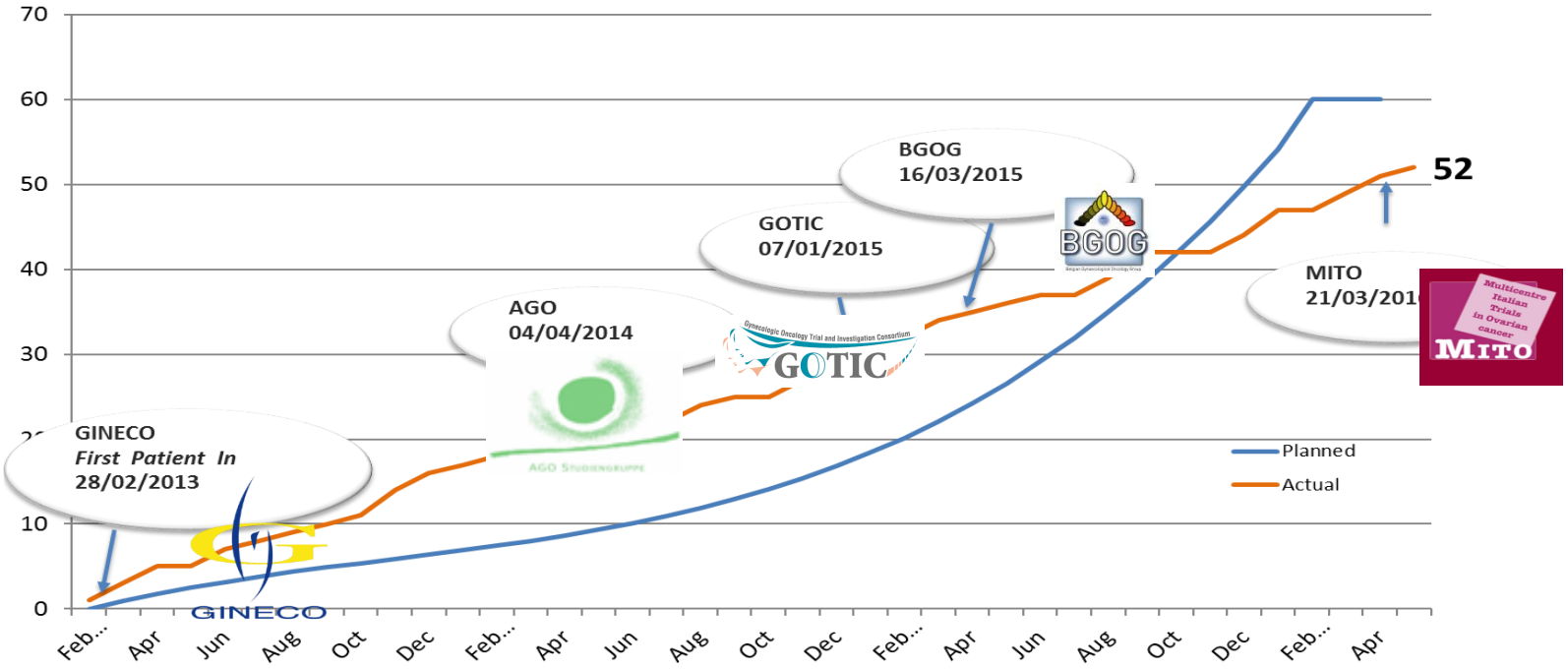
A randomized, open label, phase II trial of bevacizumab plus weekly paclitaxel followed by maintenance with bevacizumab monotherapy versus weekly paclitaxel followed by observation in patients with relapsed ovarian sex-cord stromal tumors

ALIENOR DESIGN : 60 patients



Population :
Patients with an histologically confirmed diagnosis of ovarian sex-cord stromal tumor in relapse after a platinum-based chemotherapy.

ALIENOR Status



Second interim analysis in June 2016

Assessement of clinical benefit at 6 months of the first 40 patients

IDMC meeting scheduled on June 20th 2016

On going clinical trials

- NICCC trial 12 pts recruited
- Paragon trial :endometrial & ER/PR+ sarcoma under evaluation
- LGSC (GOG 0281) trametinib: 126/250 recruited
- IRCI/EORTC 62113-55115 for HGUS with cabozantinib maintenance after 1st line CT 5 randomized/15 registred
- IRCI/NRG LMS adjuvant :slow accrual

OCCC early stage clinical trial evaluating RT

- To summarize:

  1) MRC-NCRI group c/o M. McCormack presented a trial concept on Ov Clear Cell at GCIG Rare Tumours Committee in Chicago;

- RTWG :
  - Data from the JGOG to improve inclusion criteria & hypothesis
  - McCormack (NCRI) sent a GCIG survey related to ov clear cell trial issues

JGOG

GYNECOLOGIC CANCER INTERGROUP
An Organization of International Cooperative Groups for Clinical Trials in Gynecologic Cancers

JGOG3017/GCIG Trial

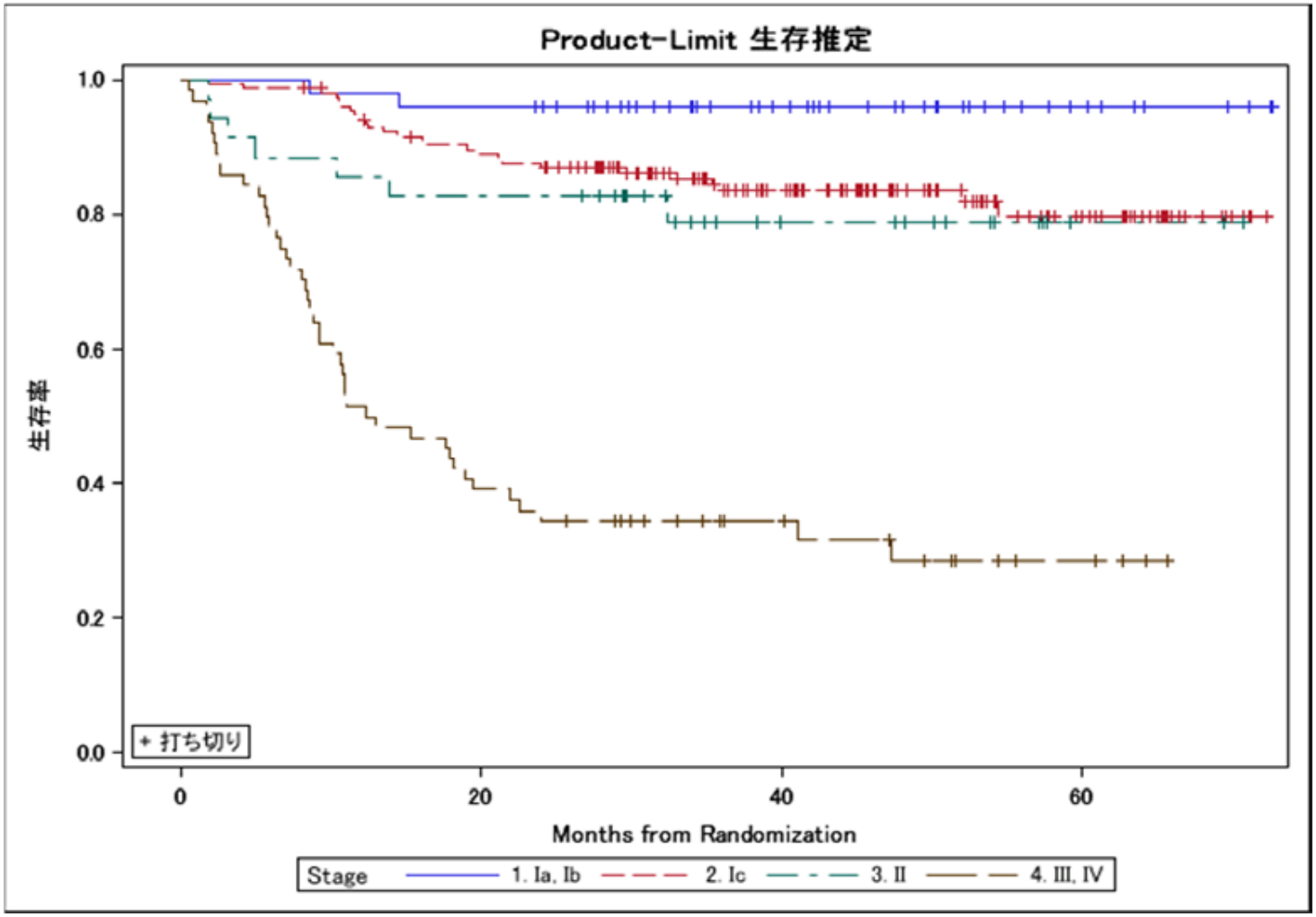
Randomized Phase III Trial of Paclitaxel plus Carboplatin (TC) Therapy versus Irinotecan plus Cisplatin (CPT-P) Therapy as First Line Chemotherapy for Clear Cell Carcinoma of the Ovary

Aikou Okamoto[*1], Toru Sugiyama[*2], Tetsutaro Hamano[*3], Jae-Weon Kim[*4], Byoung-Gie Kim[*5], Takayuki Enomoto[*6], Daisuke Aoki[*7], Yasuhisa Terao[*8], Nao Suzuki[*9], Mikio Mikami[*10], Nobuo Yaegashi[*11], Kiyoko Kato[*12], Hiroyuki Yoshikawa[*13], Sandro Pignata[*14], Jerome Alexandre[*15], John Green[*16], Seiji Isonishi[*1], Fumitoshi Terauchi[*17], Keiichi Fujiwara[*18], Kazunori Ochiai[*1]

[*1]Jikei University, [*2]Iwate Medical University, [*3] H-STAT, [*4]Seoul National University, [*5]Sungkyunkwan University, [*6]Niigata University, [*7]Keio University, [*8]Juntendo University, [*9]St.Marianna University, [*10]Tokai University, [*11]Tohoku University, [*12]Kyushu University, [*13]University of Tsukuba, [*14]Istituto Nazionale Tumori di Napoli, [*15]Hopital Hotel Dieu, [*16]University of Liverpool, [*17]Tokyo Medical University, [*18]Saitama Medical University International Medical Center

PRESENTED AT: ASCO 50th ANNUAL MEETING SCIENCE & SOCIETY

JGOG3017 PFS (TC-arm only)
IA/B vs IC vs II vs III/IV



IC3/II First recurrent sites (3017)

58%

	IC3 (n=70)	II (n=103)	total (n=173)
recurrence	n=20 (29%)	n=28 (27%)	n=48 (28%)
Peritoneal metastasis	13	15	28
Hematogenous metastasis	4	7	11
Lymph node metastasis	6	12	18
Others	1	1	2

Retrospective Analysis on Recurrent Sites in 277 Stage I Ovarian Clear Cell Carcinoma

Sou HIROSE[1)], Hiroshi TANABE[1)], Youko NAGAYOSHI[2)], Chikage NARUI[4)], Kayo SUZUKI[5)], Masahiro EZAWA[1)], Hirokazu OZONE[1)], Motoaki SAITOU[2)], Hirokuni TAKANO[1)], Seiji ISONISHI[4)], Kazuhiko OCHIAI[3)], Aikou OKAMOTO[2)]

1) Jikei University Kashiwa Hospital
2) Jikei University Hospital
3) Jikei University Katsushika Medical center
4) Jikei University Daisan Hospital
5) Dokkyo Medical University Koshigaya Hospital

CORRELATION stage & relapse

	N	%	Relapsed pts (n)	Relapsed %
IA/B	75	27	5	6
IC1	127	46	15	12
IC2	19	7	4	21
IC3	52	19	15	29
Total	**277**	**100%**	**39**	**14%**

First recurrent sites (n=39)

Peritoneal metastasis	25/39 (64%)
pelvic site 49%	
Hematogenous metastasis	12/39 (31%)
Lymph node metastasis	6/39 (15%)
Others	4/39 (10%)

Ovarian Clear Cell Trial Proposals – Stage IC2/3 & II

Chicago 2016

Mary McCormack - NCRI

GCIG and Other responders

Group	No. of responses
ICORG	1
AGO	2
NOGGO	1
MITO	1
PMHC*	1
CCTG*	1
SGCTG^	1
NCRI^	1

Group	No. of responses
KGOG	6
GOTIC	1
GINECO	1
BGOG	1
GEICO	1
ANZGOG	1
G-GOC	1
Singapore	1
Hong Kong	1

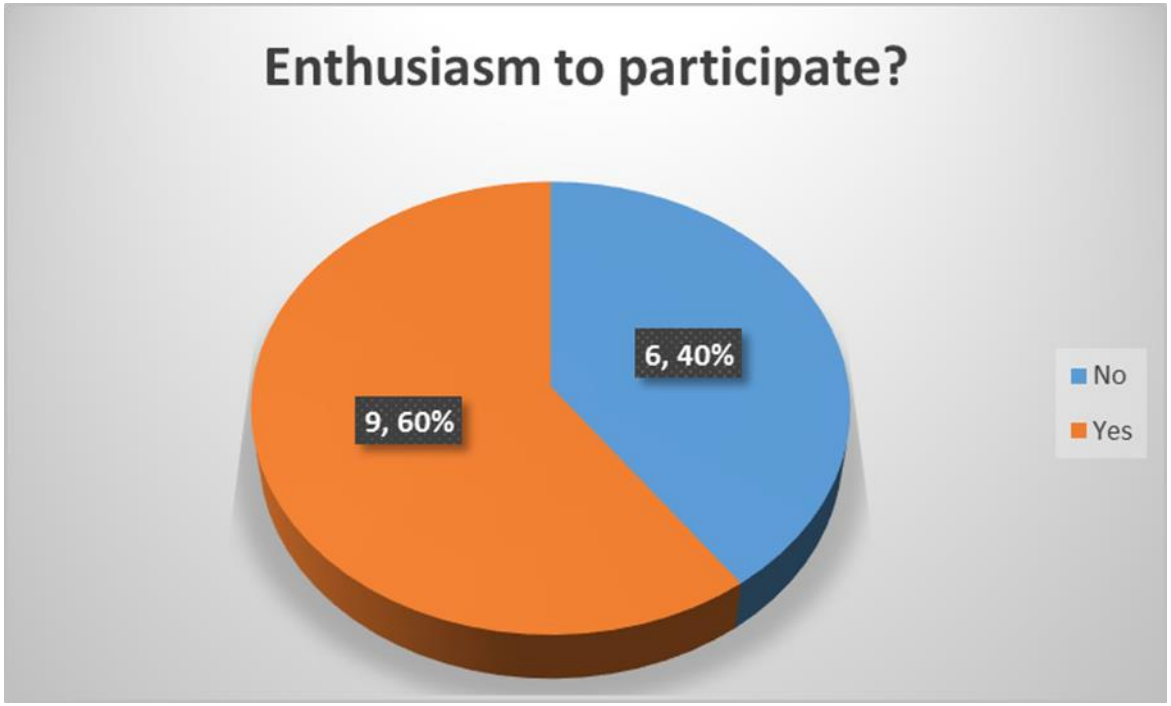
*Canadian counted as 1 response

^ UK counted as 1 response

TOTAL 15 responders

Survey Results

- Q2. Would there be enthusiasm to participate in a Clear Cell trial in your organisation?

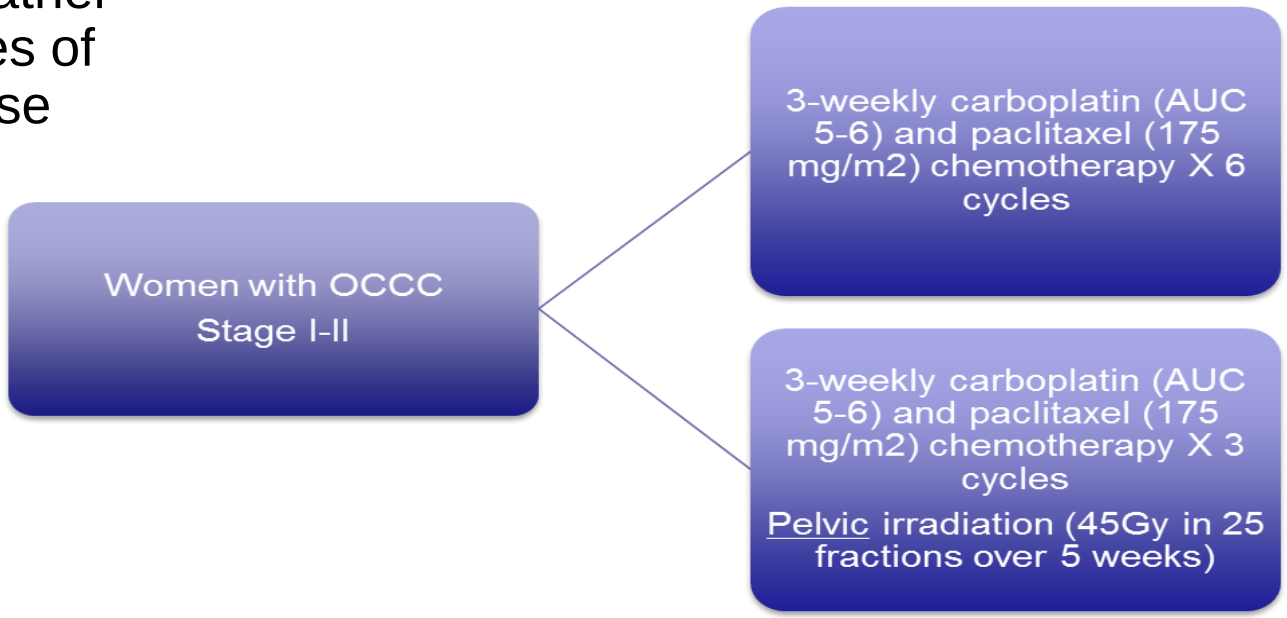


Survey Results

- Of the 3 proposals, Number 3 was the most popular (due to chemo in both arms)

Proposal 3 New Design

Preference for upfront randomisation (rather than after 3 cycles of chemo) and Phase II/III design



HR~0.6
N~300

Survey Results

GCIG	Approximate Total (per year)
ICORG	6
MITO	7
NOGGO	10
NCRI (inc SGCTG)	10
KGOG	10
ANZGOG	8
Singapore	4
Hong Kong	5
CCTG & PMHC	10
TOTAL*	**70 PER YEAR** N~230 (3-4 years to accrue) or if N~300 (4-5 years to accrue)

* Might still be possible to design a seamless phase II/III trial with this design, in which case the stats would need to be reviewed.

Next Steps

- Joint Collaboration with Anna Tinker (CCTG)
- With the support of the GCIG groups that responded positively to the survey, proposal 3 will be developed
- Some concerns on number of chemo cycles in RT arm too few (3). 4 cycles carbo/Taxol in RT arm would be a compromise

- Any other groups that wish to participate please contact Laura Farrelly or Mary McCormack

l.farrelly@ucl.ac.uk mary.mccormack@uclh.nhs.uk

KGOG
Korean Gynecologic Oncology Group

Prospective study evaluating a strategy of surgery alone and surveillance in FIGO stage I malignant ovarian germ cell tumor (KGOG 3033)

Investigators/Collaborators:

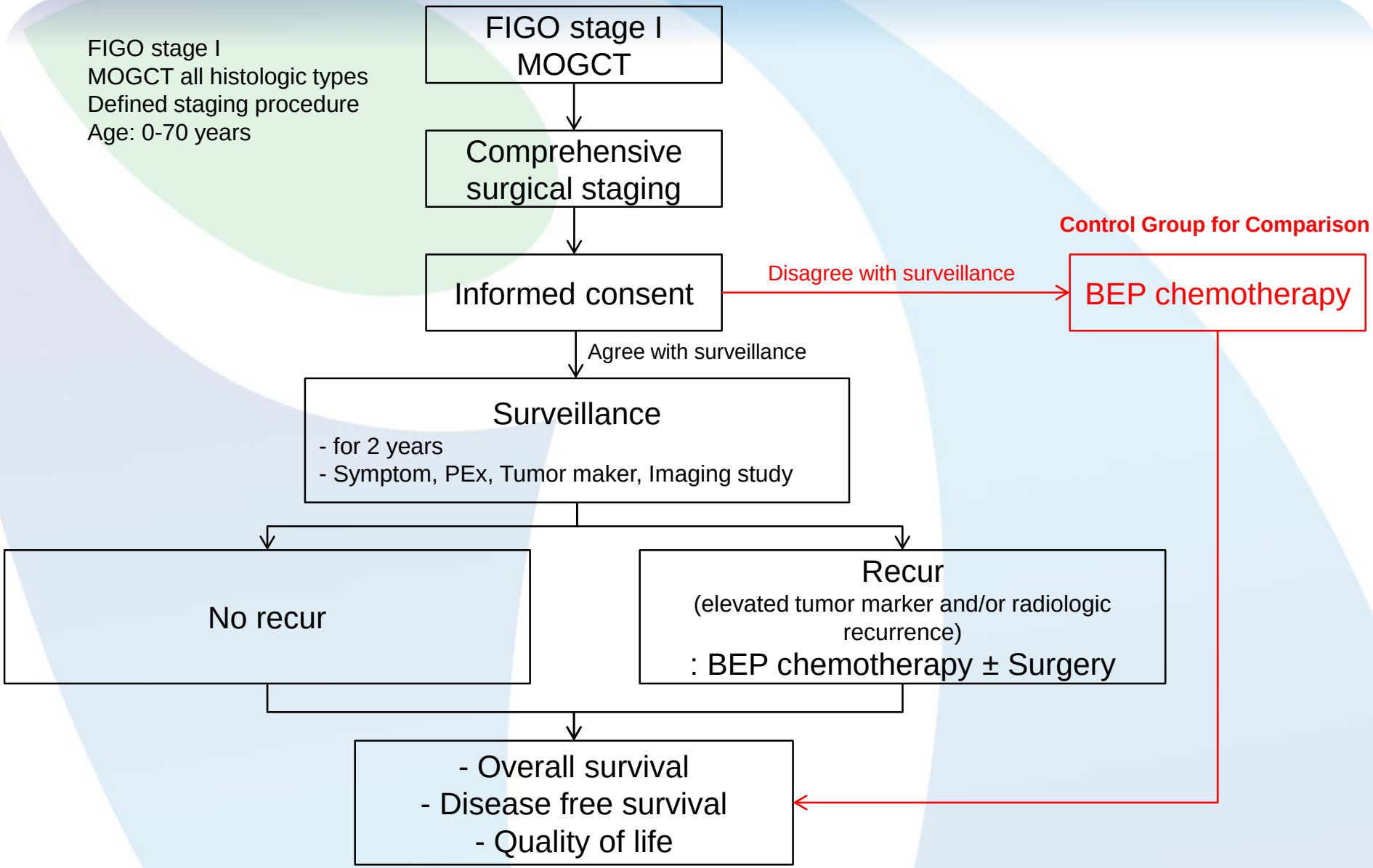
Jeong-Yeol Park, M.D., Ph.D.

Department of Obstetrics and Gynecology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea

Study outline

Prospective study evaluating a strategy of surgery alone and surveillance in FIGO stage I malignant ovarian germ cell tumor

FIGO stage I
MOGCT all histologic types
Defined staging procedure
Age: 0-70 years



“To d GCIG

- Revision of the protocol

  GCIG query 1) The extent of surgical staging

  GCIG query 2) Schedule of visit/markers/CT-scan for surveillance

  GICG query 3) Statistical plan is confirmed to select primary objective is 2 year overall survival

  - ! too many Stage IA patients (esp dysgerminoma)

  GCIG query 4) Data registry will allow data on long term follow up will be collected

  GCIG query 5) dedicated endpoints to PROs were now included EORTC QLQ-c30 and ov24 + for adult patients, sexual activity questionnaire will be surveyed 3 and 6 months after surgery.

  GCIG query 6) Get consent for patients not wishing to go on surveillance so that outcome data (especially tox) can be collected

- To participate please contact :

  Jeong-Yeol Park KGOG catgut1-0@daum.net

GCIG SCCOHT Project

- **Summary :**
  - Steering Committee: Clinicians, pathologist, scientist, study coordinator (operations), statistician
  - International Registry (prospective & retrospective)
  - Biorepository for TR
  - Registration for efficacy on all CT regimen used (1st line therapy)

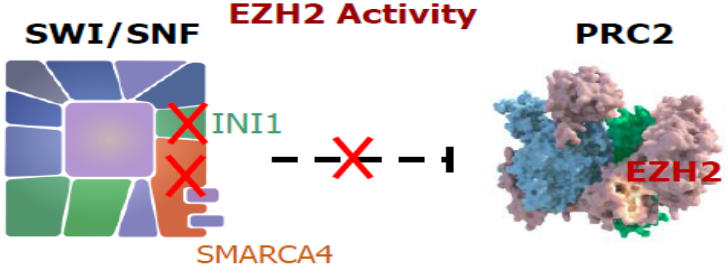
Epizyme

Personalized Therapeutics • The Power of Epigenetics

Tazemetostat

Tazemetostat (EPZ-6438): Potent and Selective EZH2 Inhibitor with Anti-Tumor Activity in SWI/SNF Mutated Rhabdoid Tumors

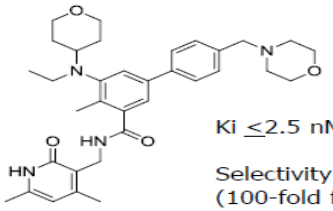
SWI/SNF Inactivation In Cancer Can Create an Oncogenic Dependency on EZH2 Activity



Loss of SWI/SNF Activity Through INI1 or SMARCA4 Mutation Causes Hyper-repression of PRC2 Target Genes

Oncogenic Transformation Dependent on EZH2 Activity

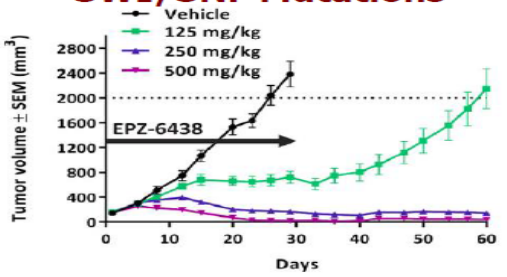
Tazemetostat: An Potent and Selective EZH2 Inhibitor with a Novel Structure



Ki ≤2.5 nM

Selectivity >20,000-fold (100-fold for EZH1)

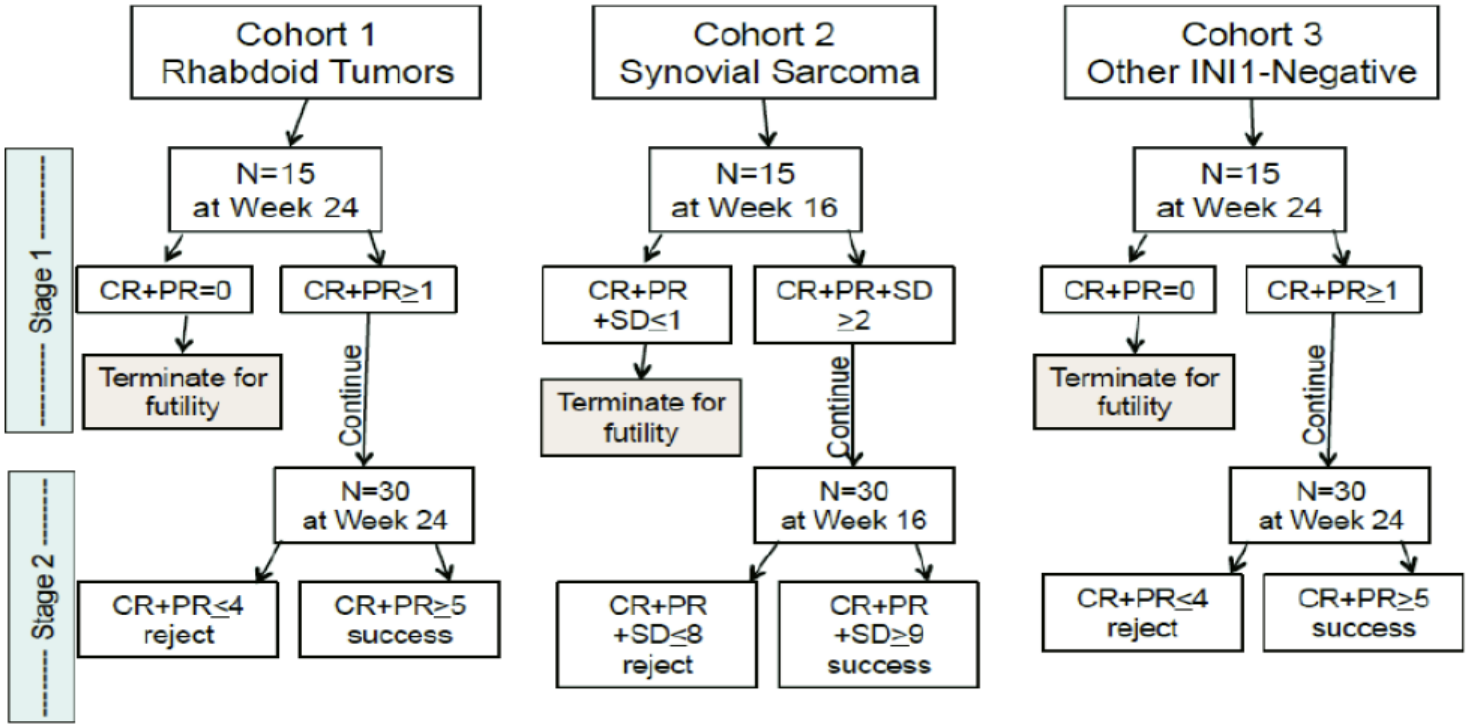
Antitumor Activity in Preclinical Models of Rhabdoid Tumors with SWI/SNF Mutations



Phase II

Study Design

EHZ-202 Study Design Schematic



N=number of subjects. CR=Complete Response. PR=Partial Response. SD=Stable Disease.

SCCOHT, next steps

- National databases
- 1st registry including retrospective data (2006) on treatments & survival 1st line & relapse + availability of tumors +/- blood
  - Important issue for informed consent :
    - Declaration of Helsinki- informed consent: « There may be exceptional situations where consent would be impossible or impracticable to obtain for such research. In such situations the research may be done only after consideration and approval of a research ethics committee."
- Prospective recruitment
- CRF validated
- MITO, NOGGO, BGOG & GINECO will participated
- Other groups interested ?
- Work will be share with the megadatabase program

In parallel, REDCap proposal (C Scott)

- BioGrid Australia, draft data collection forms for a generic rare cancer database using the REDCap platform
- This will be developing this for use in Australia for a number of rare cancer studies.
- **A generic rare cancer database using the REDCap platform**

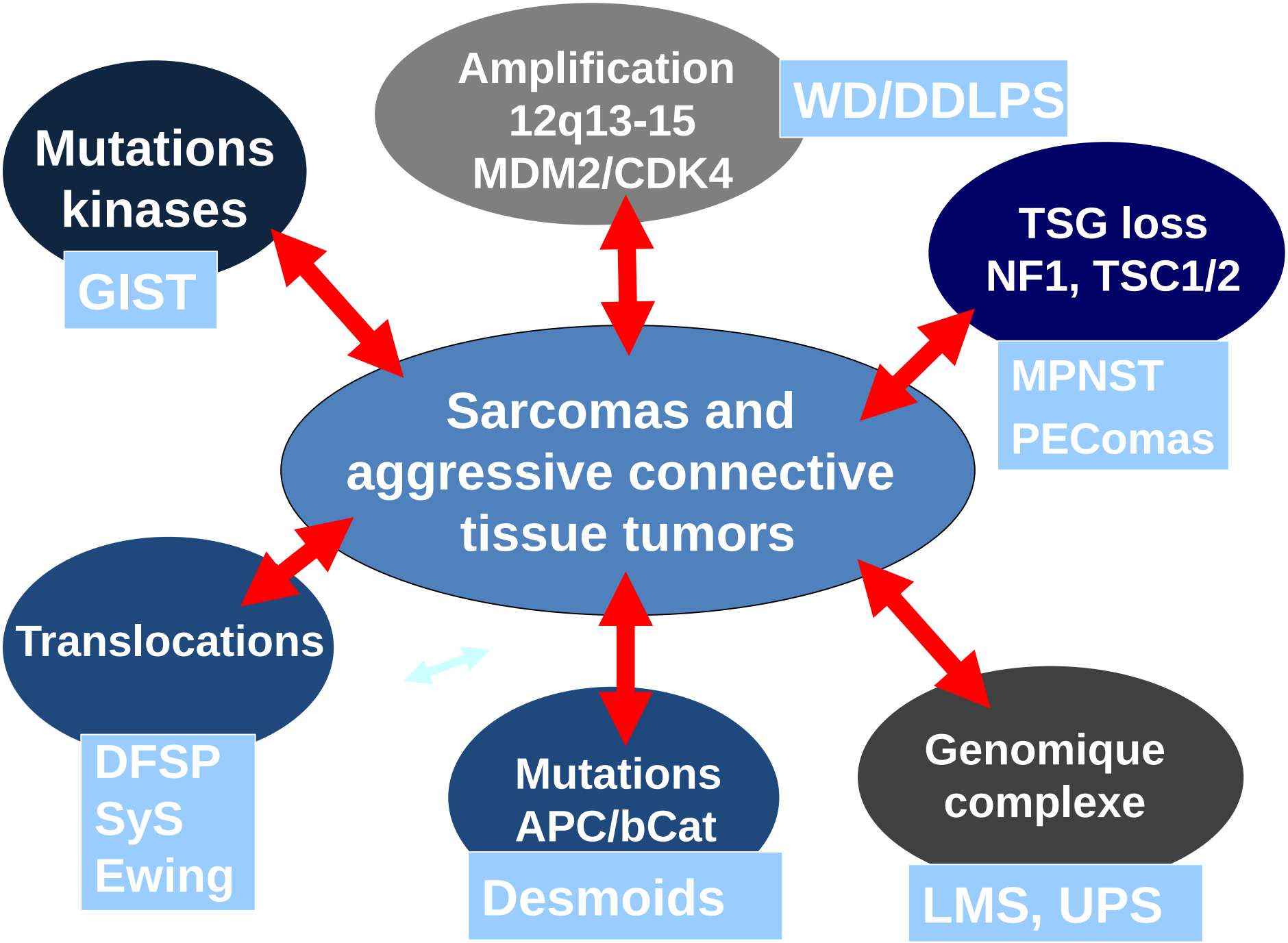
  1) this is designed for the REDCap database capability - on the screen all repeats will be hidden.
  2) all drop downs will be hidden until needed
  3) options from the appendices will work with auto-text typing options
- tumor type is left open as free text as the appendix is too long to include
- paper or database forms.
- BioGrid Australia can provide more information about that in the future.

- Program will be summit to the Megadatabase committee for comments

Clinical trials in rare tumors Challenges, successes, and failures

JY Blay

Medical Oncology
Director General Centre Leon Berard
Université Claude Bernard Lyon 1
LYRIC DGOS-INCA-4664, Devwecan Labex 061
NETSARC, RREPS


Amplification
12q13-15
MDM2/CDK4
WD/DDLPS
Mutations
kinases
GIST
TSG loss
NF1, TSC1/2
MPNST
PEComas
Sarcomas and
aggressive connective
tissue tumors
Translocations
DFSP
SyS
Ewing
Mutations
APC/bCat
Desmoids
Genomique
complexe
LMS, UPS

Take Home message

- Rare and multiple heterogeneous subtypes and molecular subtypes (N>100)
- Successes in rare entities when biology is solid
- Intergroup + light & reactive structures
- Sharing the work across members/ groups
- For memory they have conducted a clinical trial across Atlantic ☺