GCIG RTWG meeting
London Nov. 2013

Incidence & prevalence by sites

Table 3. Incidence and prevalence of rare and common cancers by site in EU27

		Incidence rate per 100,000	Standard error	Estimated incident cases in EU27	Incidence distribution (%)	Prevalence per 100,000	Standard error	Estimated prevalent cases in EU27	Prevalence distribution (%)
Common	Digestive tract	76,1	0,1	380 565	67	400,3	1,2	2 001 514	84
Rare	Digestive tract	17,2	0,1	86 143	15	50,0	0,4	250 005	11
All	Digestive tract	114,1	0,1	570 236	100	474,6	1,4	2 373 151	100
Common	Respiratory tract	31,6	0,1	157 903	49	56,2	0,3	280 918	43
Rare	Respiratory tract	13,6	0,0	68 125	21	60,2	0,4	300 876	46
All	Respiratory tract	64,1	0,1	320 391	100	130,0	0,6	649 911	100
Common	Skin	61,3	0,1	306 427	96	744,6	1,5	3 722 876	95
Rare	Skin	1,5	0,0	7 487	2	14,8	0,3	74 116	2
All	Skin	63,7	0,1	318 615	100	779,7	1,5	3 898 655	100
Common	Breast	47,7	0,1	238 471	74	522,6	4,1	2 612 913	75
Rare	Breast	4,9	0,0	24 415	8	56,9	0,7	284 484	8
All	Breast	64,3	0,1	321 429	100	700,1	6,3	3 500 252	100
Common	Female genital tract	9,6	0,0	47 779	32	126,7	0,6	633 546	38
Rare	Female genital tract	16,1	0,0	80 669	55	176,2	0,8	881 107	53
All	Female genital tract	29,5	0,1	147 597	100	331,7	1,1	1 658 589	100
Common	Male genital tract	40,6	0,1	202 224	78	270,5	1,4	1 297 655	70
Rare	Male genital tract	4,3	0,0	21 673	8	93,0	0,8	465 225	23
All	Male genital tract	52,0	0,1	259 868	100	399,6	1,6	1 997 975	100
Common	Urinary system	25,9	0,1	129 253	78	202,2	0,7	1 011 037	85
Rare	Urinary system	2,5	0,0	12 693	8	18,5	0,4	92 689	8
All	Urinary system	33,1	0,1	165 457	100	238,7	0,8	1 193 504	100
Common	Haematopoietic system	11,1	0,0	55 273	50	59,0	0,5	295 022	48
Rare	Haematopoietic system	9,6	0,0	48 077	44	62,5	0,5	312 462	50
All	Haematopoietic system	21,9	0,1	109 721	100	123,9	0,7	619 550	100
Common	All sites	309,6	0,2	1 548 036	61	2428,2	4,9	12 141 163	68
Rare	All sites	97,1	0,1	485 697	19	797,3	2,0	3 986 679	22
All	All sites	503,6	0,3	2 518 108	100	3565,4	7,2	17 826 767	100

GCIG RTWG meeting
London Nov. 2013, first step

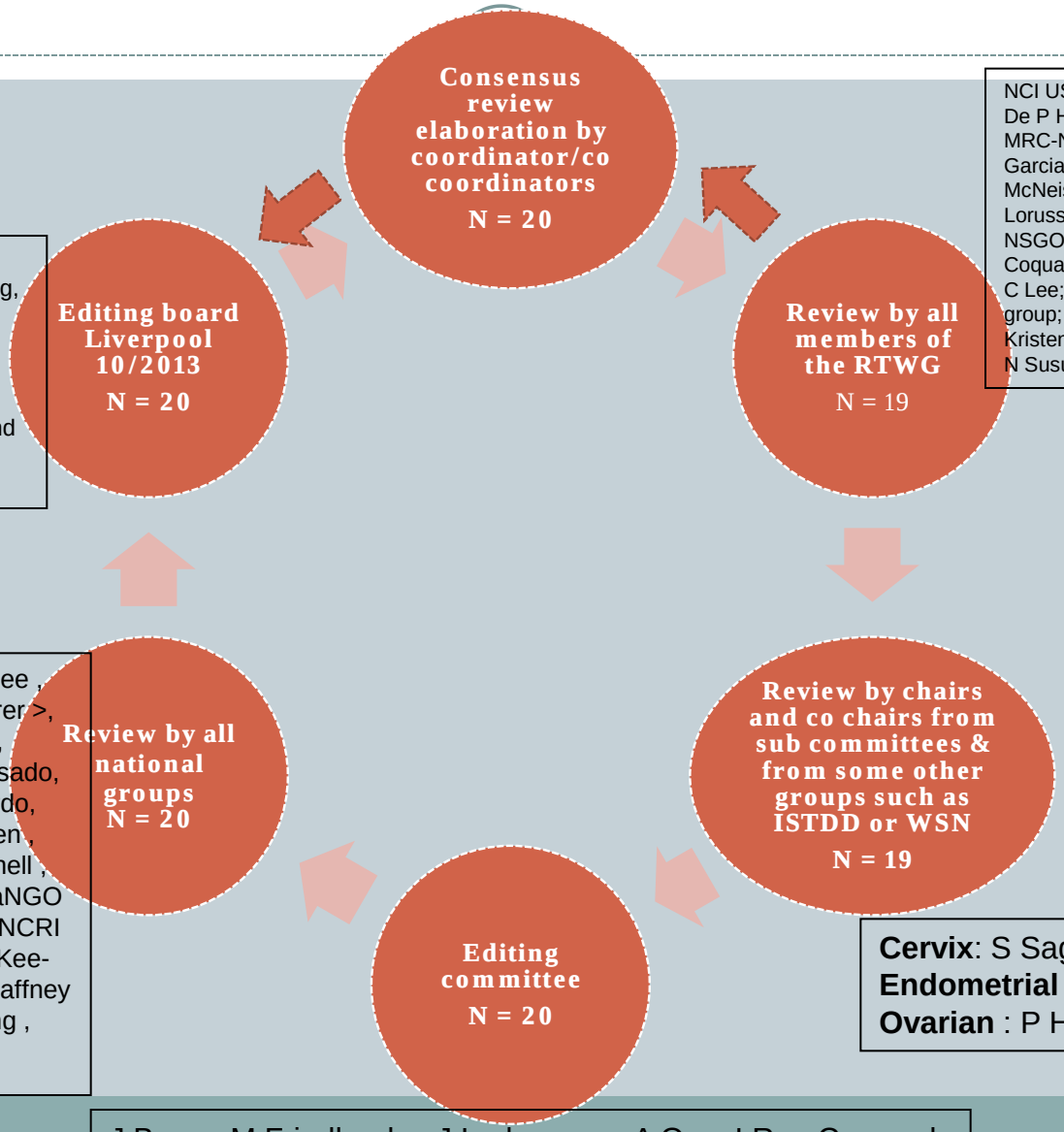
Objectives:

- To define current recommendations for rare gynecologic tumors;
- To help to define control arm for present and future clinical trials involving rare cancer;
- To identify national & international barriers for trials dedicated to rare gynecologic cancers
- To summarize and prioritize key issues for research and agree new set of trial concepts to address the key issues in several rare tumors
- To prioritize and design 3 international initiatives in rare gynecologic cancer

GCIG consensus reviews update

GCIG consensus review	leader Group	Coordinator	Co Coordinator	step
Ov & Ut carcinosarcoma	GINECO	D Berton Rigaud		sent to all groups for definitive validation
low malignant potential tumors	AGO	P Harter		sent to all groups for definitive validation
low grade serous carcinoma	GOG	D Gershenson	C Gourley	sent to all groups for definitive validation
Sex cord tumor	GINECO	I Ray Coquard	N Colombo	sent to all groups for definitive validation
germ Cell Tumor	GOG	J Brown	M Seckl	sent to all groups for definitive validation
squamous Ov carcinoma	SGCTG	R Glasspool	Antonio Gonzales	sent to all groups for definitive validation
Small Cell carcinoma cervix	GOTIC	K Fujiwara	N Reed	sent to all groups for definitive validation
small cell carcinoma OV	EORTC	N Reed	P Pautier	sent to all groups for definitive validation
vulvar & vagina melanoma	US NCI	M Leitao	Xi Cheng	sent to all groups for definitive validation
ovarian carcinoid tumor	GICOM	N Reed	E Gomez	sent to all groups for definitive validation
Mucinuous carcinoma	MRC/NCRI	J Ledermann	J Brown	sent to all groups for definitive validation
clear cell carcinoma Ovary	JGOG	A Okamoto	R Glasspool	sent to all groups for definitive validation
clear cell carcinoma Cervix & Ut	GOTIC	K Fujiwara & Dr Hasegawa		sent to all groups for definitive validation
trophoblastic diseases	MITO	K Larusso	M Seckl	sent to all groups & ISTDD validation
low grade endometrial stromal sarcoma	EORTC	F Amant		sent to all groups for definitive validation
HG uterine sarcoma	GINECO	P Pautier		sent to all groups for definitive validation
uterine serous carcinoma	JGOG	S Sagae	A Viswanathan	sent to all groups for definitive validation
adenosarcoma	ANZGOG	M Friedlander		sent to all groups for definitive validation
Ut & Ov leiomyosarcoma	US NCI	M Hensley		sent to all groups for definitive validation
glandular carcinoma of cervix	GOTIC	K Fujiwara	B Monk	sent to all groups for definitive validation

Delineated Process



J.Brown, P.Pautier, M.Hensley, F.Amant, M.Leitao, B.Rigaud, X.Cheng, N.Reed, P.Harter, D.Gershenson, C.Gourley, N.Colombo, R.Glasspool, A.Gonzalez, K.Fujiwara, E.Gomez, A.Okamoto, K.Lorusso, Susumu for S.Sagae, A.Viswanathan, M.Seckl, and M.Friedlander,J Lederman, E Pujade-Lauraine, I Ray-Coquard, J Bryce

NCI US B Greer; NCI US T Trimble; AGO-De P Harter; ANZGOG M Friedlander; MRC-NCRI C Gourley; GICOM EM Gomez Garcia; MRC-NCRI A Clamp; MRC-NCRI I McNeish; ANZGOG D Rischin; MITO K Lorusso; G Daniele; H Hal; Blagden, SP; NSGO E Avall-Lundqvist; GINECO I Ray-Coquard, SGCTG R Glasspool; ANZGOG C Lee; C Scott; JGOG D Aoki; JGOG group; SWOG M Bookman; NSGO G Kristensen; EORTC N Ottevanger; JGOG N Susumu; G Keiichi

Group Représentatives: ACRIN S Lee , AGO Au C Marth, AGO De J Pfisterer >, ANZGOG A Brand , COGI J Berek , DGOG C Creutzberg EORTC A Casado, GEICO A Poveda, GICOM D Gallardo, GINECO AC Hardy , GOG T Thigpen , GOTIC K Fujiwara , ICORG D Donnell , JGOG D Aoki , KGOG JW Kim , MaNGO R Fossati , MITO S Pignata , MRC-NCRI J Ledermann , NCIC CTG M Fung-Kee-Fung , NSGO M Mirza , RTOG D Gaffney , SGCTG N Siddiqui , SGOG R Zang , NOGGO J Sehouli , PMHC A Oza

Cervix: S Sagae & B Monk
Endometrial : K Lorusso & S Greggi
Ovarian : P Harter & A Gonzalez

J Bryce, M Friedlander, J Ledermann, A Oza, I Ray-Coquard

What has been done

- 20 available documents (pdf version sent to you yesterday)
  - All Reviewed by MITO, AGO-D, GINECO, JGOG, GOTIC, ANZGOG, KGOG, MANGO, GEICO, SGCTG, NSGO
  - Partially reviewed by GOG, MRC-NCRI, GICOM, COGI, ICORG, NCIC CTG, RTOG, NOGGO, PMHC

Acknowledgments to authors, co authors, reviewers .... (many many many people)

A du Bois
A Evans
A Floquet
A Gonzales
A Okamoto
A Poveda
A Viswanathan
B Bui
B Monk
B Seddon
C Gourley
C Kurzeder
C Lhomme
D Aoki
D Berton Rigaud
D Gallardo
D Gershenson
D Luvero
D Mezzanzanica
D Millan
E Gomez
E Pujade-Lauraine
F Amant
F Hilpert
F Joly
F Lecuru
F Selle
G Emons
G Freyer
G Rustin
G Mangili
H Fujiwara
H Itamochi
H Nomura
I Konishi
I Ray-Coquard
I Treilleux
J Alexandre
J Brown
J Ledermann
J Martin
J Pfisterer
JE Kurtz
JW Kim
JY Blay
K Baumann
K Fujiwara
K Hasegawa
K Lorusso
L Gladieff
L Mileshkin
M Bacon
M Devouassoux
M Friedlander
M Hensley
M Leitao
M Mandai
M Quinn
M Seckl
M Takano
M Yasuda
N Colombo
N Matsumura
N Penel
N Reed
N Siddiqui
N Susumu
P Harter
P Morice
P Pautier
PO Witteveen
R Glasspool
S Bonvalot
S Greggi
S Mabuchi
S Mahner
S Pignata
S Sagae
T de La Motte Rouge
T Sato
T Takano
Xi Cheng
Y Takei

Next steps for consensus reviews documents

- Waiting for all groups revision
  - No mail sent to GCIG or authors = agreement
- Publications :
  - Rules and authorships : authors, co authors, chairs, reviewers from national groups (priority to people who work on)
  - Publications on website and in a journal
    - One paper summarizing all documents
    - 20 papers in a supplement (Int J Gyn Cancer)
- What place for rare tumors in the 5th OCCC, Japan 2015?
- The most easy part of the job is made, the next will be really more difficult (updating, implementation ...)

Part 2 (general session & break out sessions)

- **Main statistical issues for ongoing & future trials – Regulatory Issues**
- **Working groups sessions:**

1 - Relatively rare diseases (glandular carcinoma of the cervix)

- **Chair: Keiichi Fujiwara – Co chair: Ros Glasspool**
  - **Stats representative - Jim Paul;**
  - **Ops representative – Benedicte Votan.**

2 - Rare disease (carcinosarcoma of the uterus)

- **Chair: Amit Oza – Co Chair: Andres Poveda**
  - **Stats representative – Max Parmar;**
  - **Ops representative – Jane Bryce**

3 - Very rare diseases (Small cell carcinoma of the ovary)

- **Chair: David Gershenson – Co Chair: Nicoletta Colombo**
  - **Stats representative – Mark Brady;**
  - **Ops representative – Gabriele Elser**

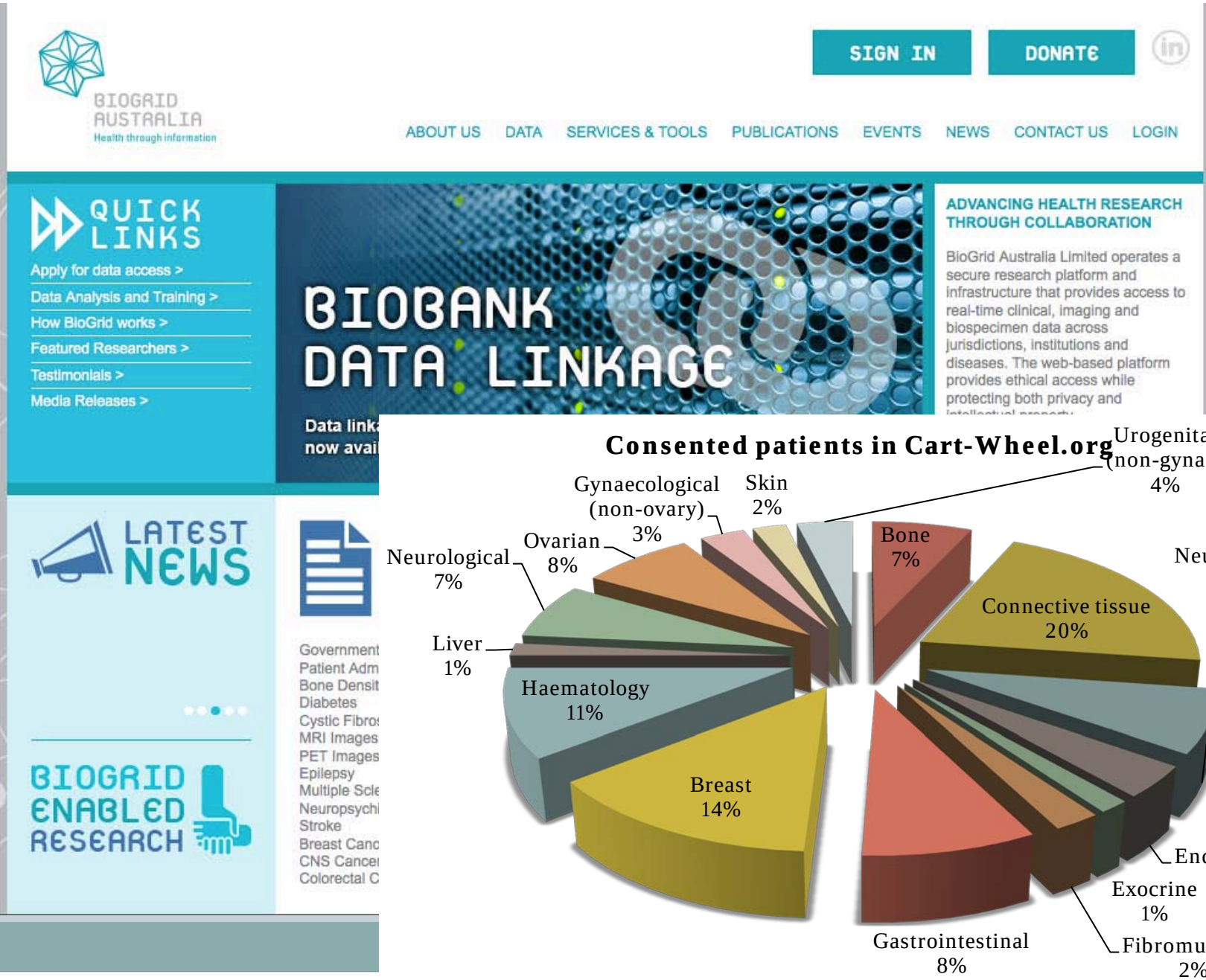
Take home message (1)

- From a statistical point of view:
  - Should not use this as an excuse to limit ambition
    - Use a **relaxed significance level**
    - Using External Evidence - Bayesian Approach –
    - Maximising information (Factorial designs, Random at several time in the same protocol, Stopping early, molecular signals) : **Consider a multi-arm, multi-stage trial**
    - Not using single arm phase II (more than 60% of potential false positive) except for very rare disease or where no active treatment is defined
- From Harmonization point of view:
  - Need to lighten the operational processes in order to decrease the budget
  - Need to be based on the **Intergroup Agreement**
  - To facilitate the recruitment by a national network of reference centres
  - Need to share some tasks between groups

Take home message (2)

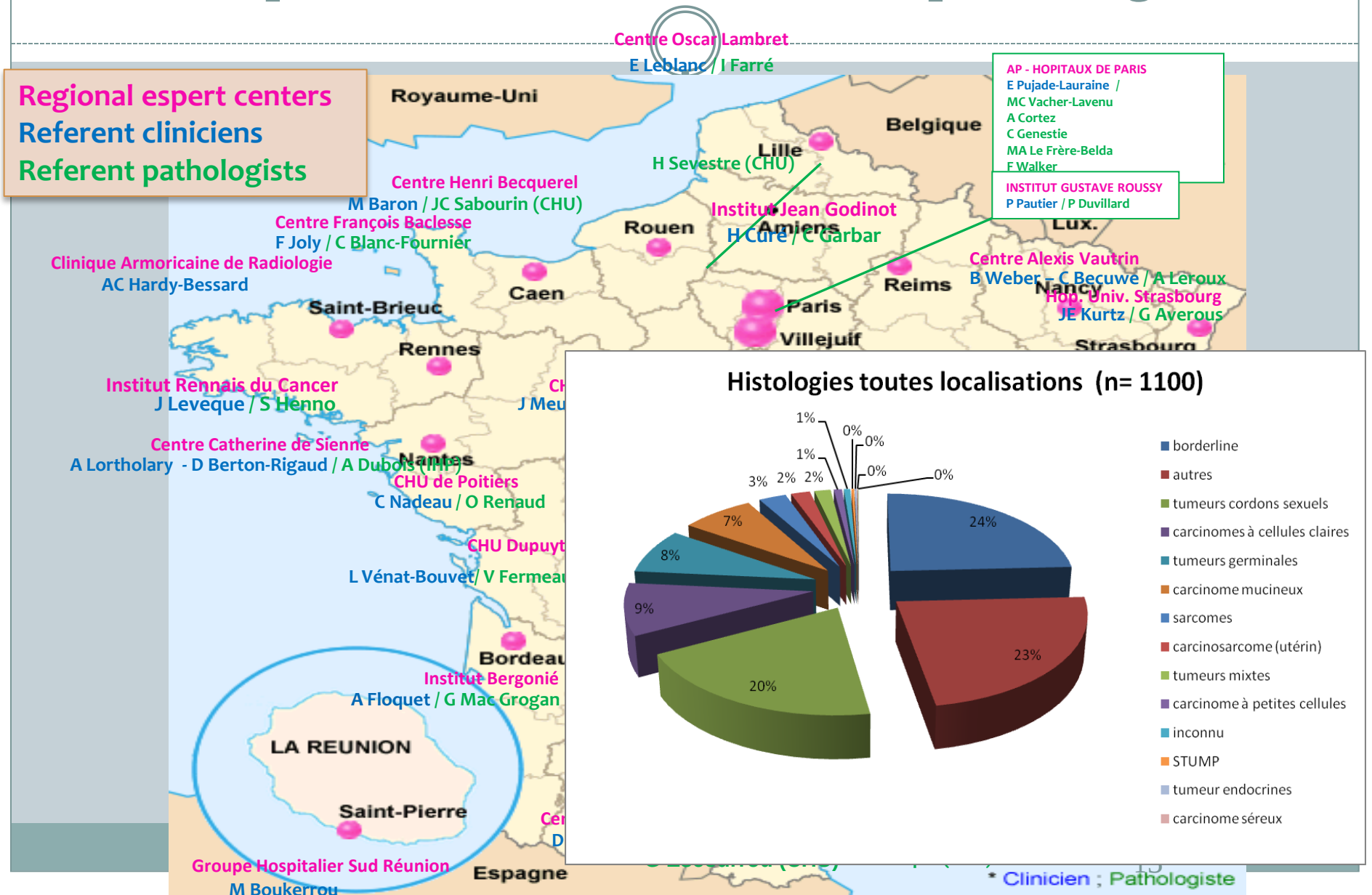
- From a international agency (IRCI) point of view:
  - Functions :
    - Work to lower barriers to performance of international clinical trials in cancer.
    - Provides a common voice for academic clinicians to approach industry for worldwide collaboration in rare cancer clinical trials.
  - But Priority to randomized trials , Audit, registry or non-trial tissue collection trials are not a priority

- From the biology point of view:
  - Experience from TCGA, particularly with governance
    - **MTA for biologic specimen need to be available**
  - Need to Identify patients with rare cancers


BIOGRID AUSTRALIA
Health through information
SIGN IN
DONATE
ABOUT US
DATA
SERVICES & TOOLS
PUBLICATIONS
EVENTS
NEWS
CONTACT US
LOGIN
QUICK LINKS
Apply for data access >
Data Analysis and Training >
How BioGrid works >
Featured Researchers >
Testimonials >
Media Releases >
BIOBANK DATA LINKAGE
ADVANCING HEALTH RESEARCH THROUGH COLLABORATION
BioGrid Australia Limited operates a secure research platform and infrastructure that provides access to real-time clinical, imaging and biospecimen data across jurisdictions, institutions and diseases. The web-based platform provides ethical access while protecting both privacy and
LATEST NEWS
BIOGRID ENABLED RESEARCH
Government
Patient Adm
Bone Densit
Diabetes
Cystic Fibro
MRI Images
PET Images
Epilepsy
Multiple Scle
Neuropsychi
Stroke
Breast Canc
CNS Cancer
Colorectal C
Consented patients in Cart-Wheel.org
Urogenital (non-gynae) 4%
Skin 2%
Gynaecological (non-ovary) 3%
Ovarian 8%
Neurological 7%
Liver 1%
Haematology 11%
Breast 14%
Gastrointestinal 8%
Fibromuscular 2%
Exocrine 1%
Endocrine 4%
Neuroendocrine 8%
Connective tissue 20%
Bone 7%

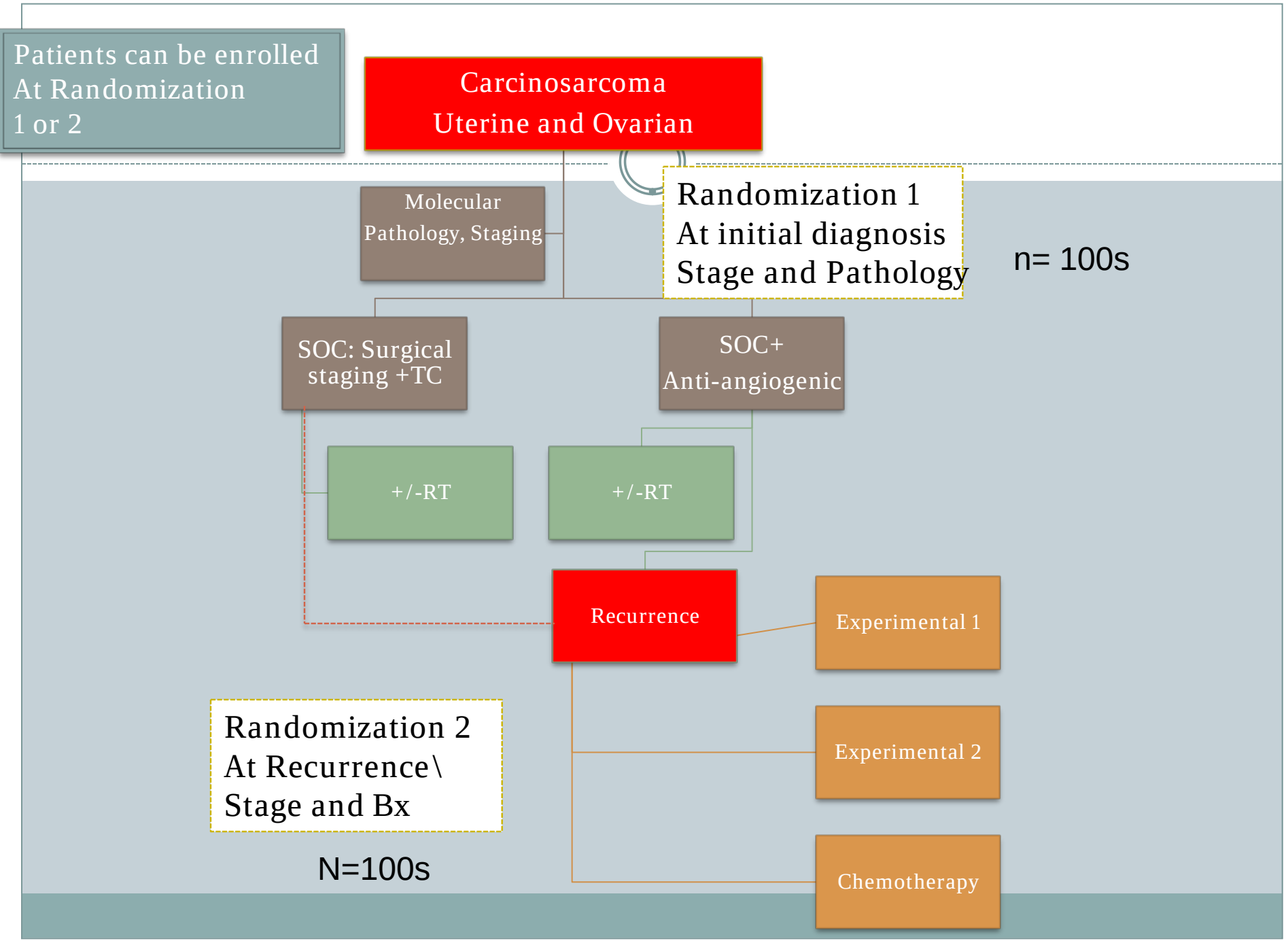
Structuration of the national network
24 expert centers and referent pathologists

Regional espert centers
Referent cliniciens
Referent pathologists

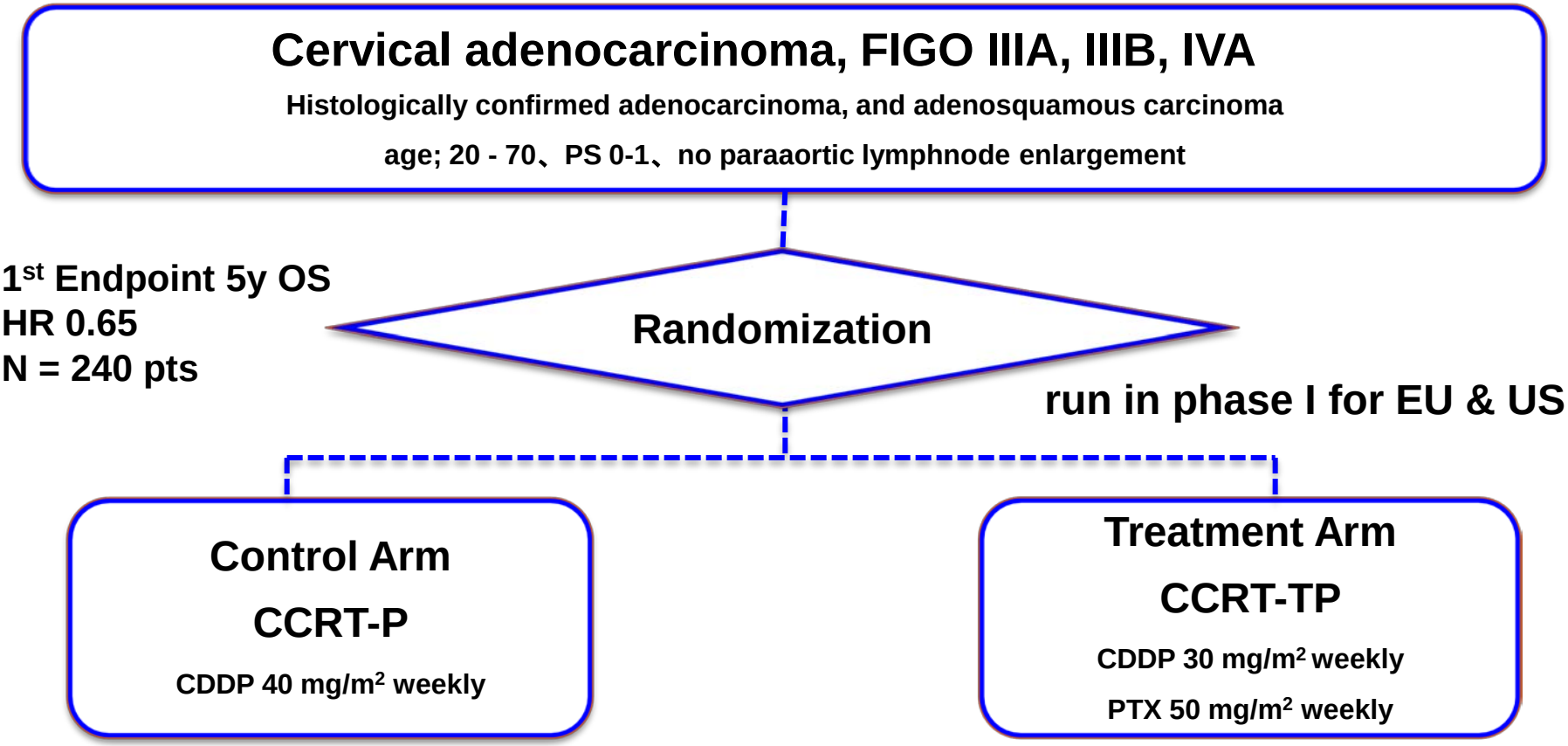


What have we achieved yesterday?

- 20 validated documents
- 3 Projects:
  - Very rare tumors: a registry study starting with SCC (ovary) including clinical data and tissue
    - Retrospective & prospective with standard databases & multidisciplinary approach & generate proofs of principle genomics
  - Rare tumors, carcinosarcoma (ovarian and uterine):
    - A randomized umbrella study including patients 1st line (SOC +/- anti angio) and at relapse included in 2 experimental arms vs CT
  - Relatively rare tumors: cervical adenocarcinoma:
    - Observational study for conservative surgery (stage AIS & IA1)
    - Meta analysis of on going trials dedicated to CT and anti angio
    - Phase III for IB2 to III stage (ccRT-P vs ccRT-CT) with run in phase I for EU & US + 2nd randomization for 4 x CT adj vs obs
    - Randomized discontinuation trial for targeted th in met phase.


Patients can be enrolled
At Randomization
1 or 2
Carcinosarcoma
Uterine and Ovarian
Molecular
Pathology, Staging
Randomization 1
At initial diagnosis
Stage and Pathology
n= 100s
SOC: Surgical
staging +TC
SOC+
Anti-angiogenic
+/-RT
+/-RT
Recurrence
Experimental 1
Randomization 2
At Recurrence\
Stage and Bx
Experimental 2
N=100s
Chemotherapy

A phase III clinical trial of CCRT with paclitaxel and cisplatin for local advanced cervical adenocarcinoma



Integration of systemic chemotherapy after CCRT

Second randomization

Using paclitaxel + carboplatin x4 cycles

Tissue collection recommended:

Need logistic setup under GCIG leadership

GCIG Rare Tumors project, the future

- More dedicated projects to rare gynecologic cancer

  = Limited resources imply concerted actions

  - Combination of clinical trials and other projects (specific databases & tumor collections)

- Next tasks to be delivered:
  - Publication of the consensus reviews (RTWG & Exe Co)
  - Elaboration of an GCIG International agreement for biological samples (Ops & Harm groups)
  - 3 proposals: shift to Standing committees to detail & to continue the project (Cervix, Endometrial & RTWG)