The Swiss Experience with SAKK: (Challenges and opportunities coming from a small country)

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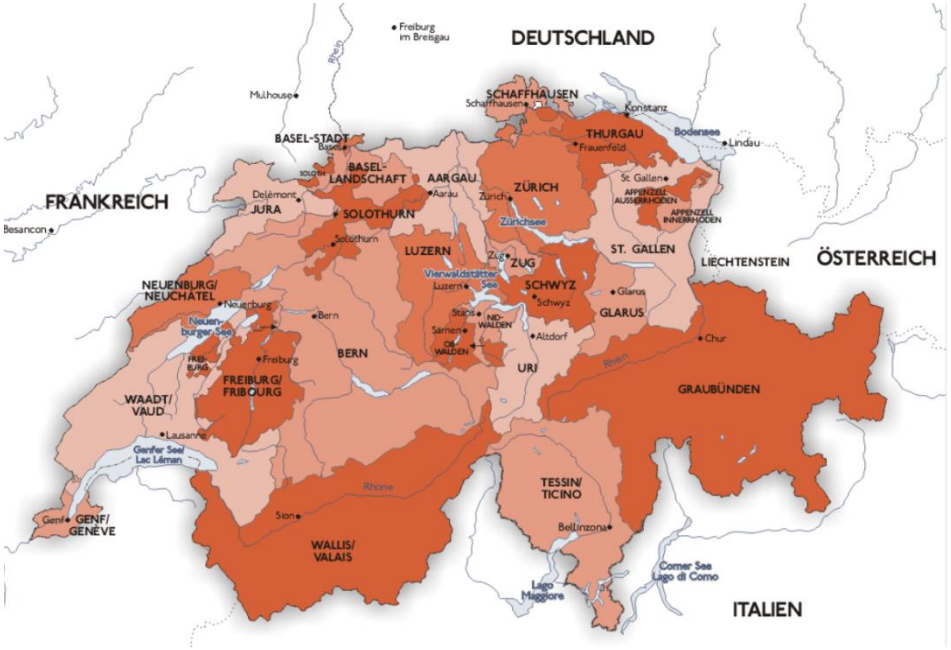
Conflicts of Interest
(last two years)

- **Personal honoraria** for participation in *advisory boards* from Amgen, MSD; *other honoraria* from Radio-televisione Svizzera Italiana (RSI), German-speaking European School of Oncology (DESO); *invited speaker* for ESMO, Swiss group for Clinical Cancer Research (SAKK), Swiss Academy of Multidisciplinary oncology (SAMO); *travel grant* from AstraZeneca.
- **Institutional honoraria** for participation in *advisory boards or in Independent Data Monitoring Committees and Steering Committees* from AAA International, Amgen, AstraZeneca, Bayer, Bristol-Myers Squibb, Modra Pharmaceuticals, MSD, Myriad Genetic, Novartis, Orion, Pfizer, Telixpharma; *other honoraria* from Silvio Grasso Consulting, WebMD-Medscape.
- Co-inventor on patent application (WO 2009138392 A1) for a method for biomarker discover (granted in China, Europe, Japan and the US)
- Deputy of the ESMO guidelines committee for GU cancers, member of the scientific committee of ESMO guidelines, member of the EAU guideline panel for prostate cancer, past chair of the EORTC GU group; Member of the STAMPEDE trial management group

Switzerland?



41 285 km^2
26 counties (cantons)
8 Mio inhabitants
4 Languages

Population in Switzerland

Rather homogenous; concept of solidarity important

Long life expectancy

High cancer incidence population

Unwillingness of patients to travel for care to larger centers, access to (also new) drugs rather easy

Swiss Clinical Research in Oncology: SAKK

SAKK

Schweizerische Arbeitsgemeinschaft für Klinische Krebsforschung
Groupe Suisse de Recherche Clinique sur le Cancer
Swiss Group for Clinical Cancer Research
Gruppo Svizzero di Ricerca Clinica sul Cancro

Founded 1965 as the clinical part of a substitute of a «NCI»
From ca. 2009 formation of GU project group
Initiation of small, non-randomized Phase II trials:

- Efficacy of cetuximab in metastatic castration-resistant prostate cancer might depend on EGFR and PTEN expression: results from a phase 2 trial (SAKK 08/07) ***Cathomas et al Clin Canc Res 2012***

- Phase 2 trial of single-agent everolimus in chemotherapy-naive patients with castration-resistant prostate cancer (SAKK 08/08) ***Templeton et al Eur Urol 2013***

PEACE consortium

European Association of Urology

2014

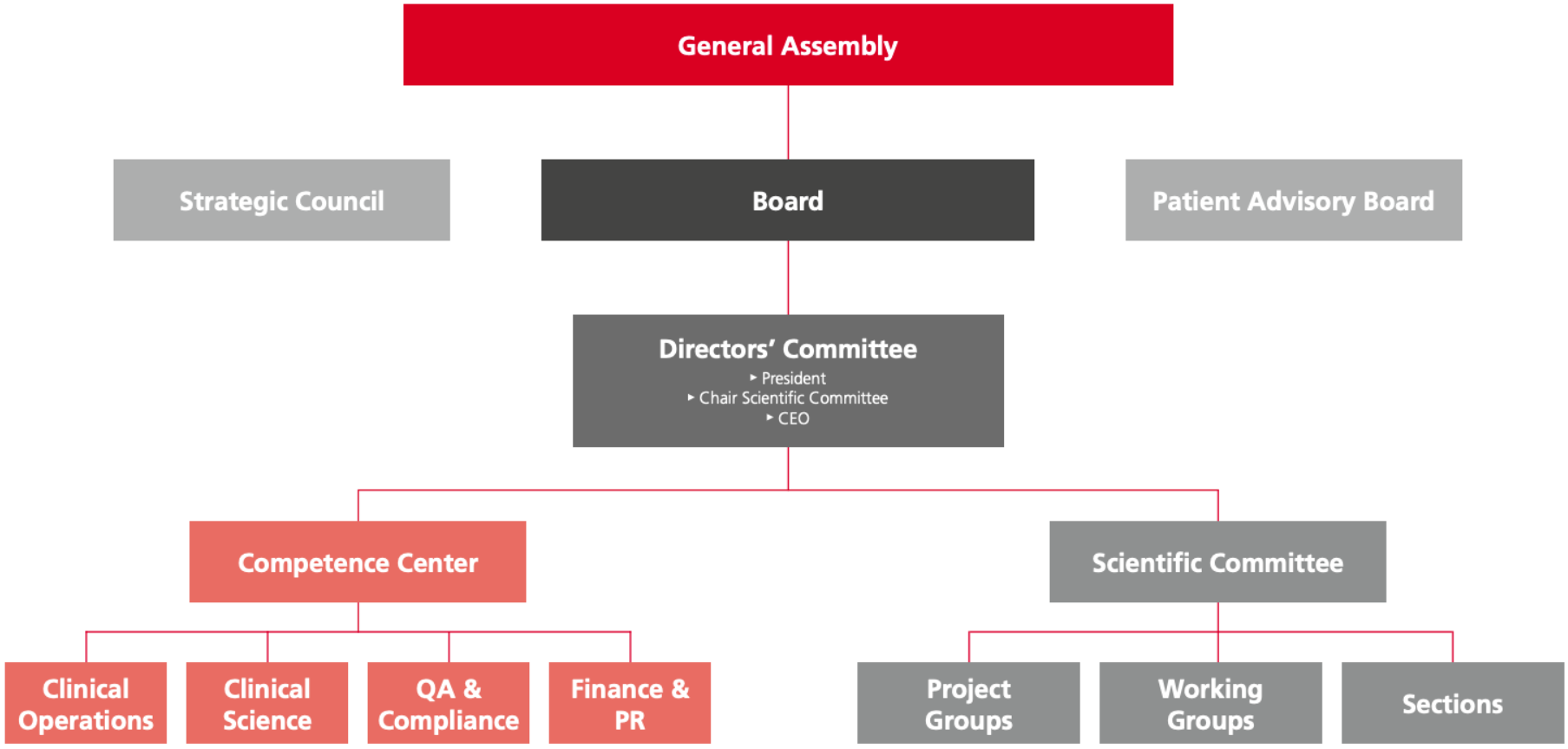
Review – Prostate Cancer

Achievements and Perspectives in Prostate Cancer Phase 3 Trials from Genitourinary Research Groups in Europe: Introducing the Prostate Cancer Consortium in Europe

Karim Fizazi[a,*], *Per-Anders Abrahamsson*[b], *Goran Ahlgren*[b], *Joaquim Bellmunt*[c], *Daniel Castellano*[d], *Stephane Culine*[e], *Ronald de Wit*[f], *Silke Gillessen*[g], *Juergen E. Gschwend*[h], *Freddie Hamdy*[i], *Nicholas James*[j], *Raymond McDermott*[k], *Kurt Miller*[l], *Thomas Wiegel*[m], *Manfred Wirth*[n], *Bertrand Tombal*[o]

SAKK: Organigram

SAKK
WE BRING PROGRESS TO CANCER CARE



European Association of Urology

Platinum Priority – Prostate Cancer
Editorial by Robert J. Hamilton on pp. 475–477 of this issue

2014

Metformin in Chemotherapy-naive Castration-resistant Prostate Cancer: A Multicenter Phase 2 Trial (SAKK 08/09)

Christian Rothermundt[a,], Stefanie Hayoz[b], Arnoud J. Templeton[a,b], Ralph Winterhalder[c], Räto T. Strebel[d], Daniela Bärtschi[b], Michael Pollak[e], Lillianne Lui[e], Kathrin Endt[f], Ralph Schiess[f], Jan H. Rüschoff[g], Richard Cathomas[d,†], Silke Gillessen[a,†]*

Randomised trials:

SAKK 08/11: Maintenance trial with Orteronel: Accrual stopped prematurely (published 2016)

SAKK 09/10: Salvage RT with 64 vs 70Gy in patients with biochemical relapse after RP

STAMPEDE: Collaboration

SAKK 96/12: Denosumab monthly versus 3-monthly

Publications of SAKK GU group last 5 years

Year	Trial	Title	
2018	STAMPEDE	RT to the primary	Parker C, LANCET
2018	STAMPEDE	Adding Abi or Doce	Sydes M, Ann Oncol
2019	STAMPEDE	Abi in high and low-risk	Hoyle A, Eur Urol
2019	SAKK 08/14	Analysis of AR/ARV7	Hench I, Cancers
2020	SAKK 06/14	Previous failure of BCG	Rentsch C, Oncoimmunology
2021	STAMPEDE	Abi +/- Enza in M0	Attard, Lancet
2021	SAKK 09/10	Dose-intensified vs conventional sRT	Ghadjar P, Eur Urol
2022	STAMPEDE	Long term Doce in M0	James N, JNCI Cancer Spectrum
2022	SAKK 01/10	Carbo and RT for IIA/B seminoma	Papachristofilou A,Lancet Oncol
2022	SAKK 06/14	Induction/maintenance BCG	Rentsch C, Eur Urol Oncol
2022	SAKK 09/10	Adherence to contouring QA	Beck M, Int J Radiat Oncol Biol Phys

Ongoing studies

SAKK 01/18

Reduced intensity radio-chemotherapy for stage IIA/B seminoma. A multicenter, open label phase II trial with two cohorts

SAKK 06/19

Muscle-invasive bladder cancer (MIBC) and perioperative treatment

SAKK 67/20

Open-label single-stage phase 1B study of a new micellar docetaxel compound in patients with advanced castration-resistant prostate cancer (CRPC)

In general for „own“ SAKK studies

Prostate Cancer:

- Focus on mCRPC state with translational research
- Salvage RT

Bladder Cancer:

- BCG and immunotherapy-oriented, perioperative state

Testicular Cancer:

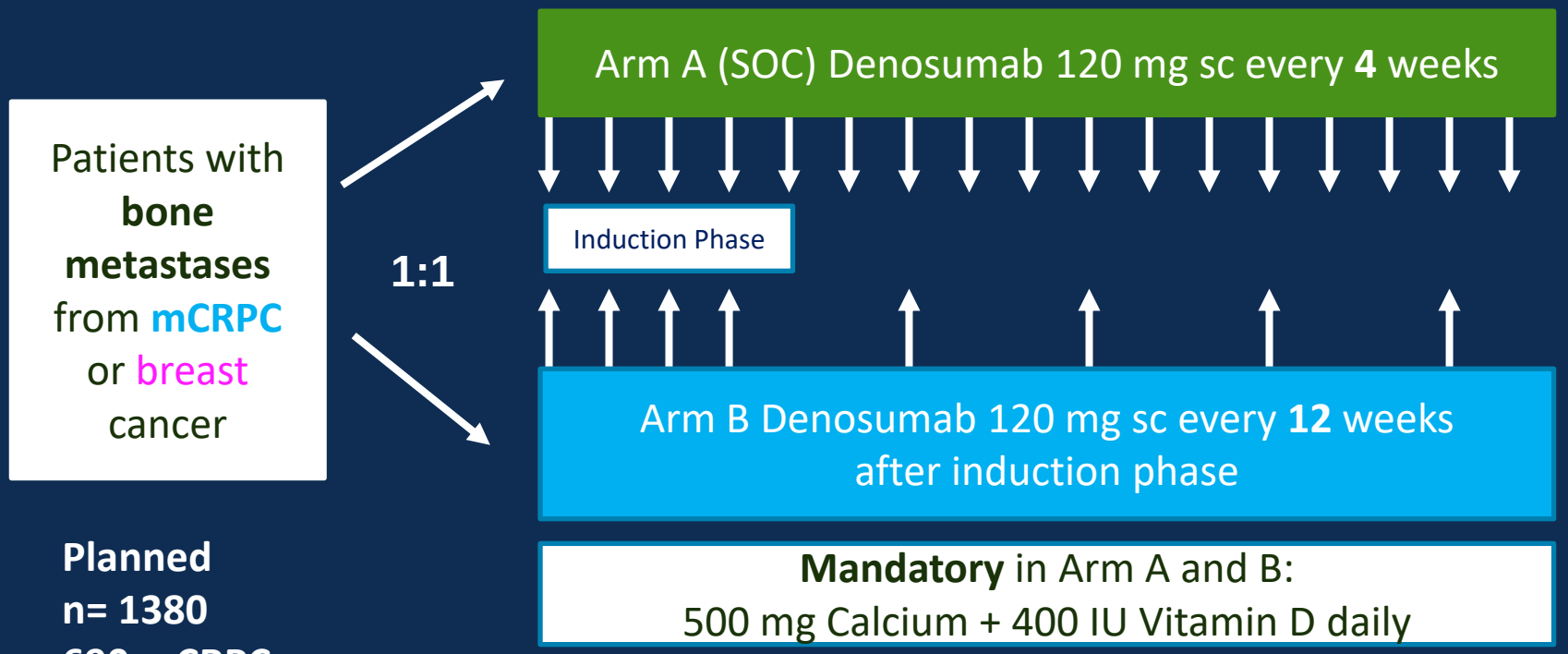
- Seminoma 2A/B

New funding opportunities

Collaboration with Santésuisse (society of private insurances):
Financing trials, that could potentially save them costs

Prevention of Symptomatic Skeletal Events (SRE) with Denosumab administered every 4 weeks versus every 12 weeks
A Non-Inferiority Phase III Trial (SAKK 96/12, REDUSE)

REDUSE: Trial Design



Planned
n= 1380
690 mCRPC

Objectives and Endpoints of REDUSE

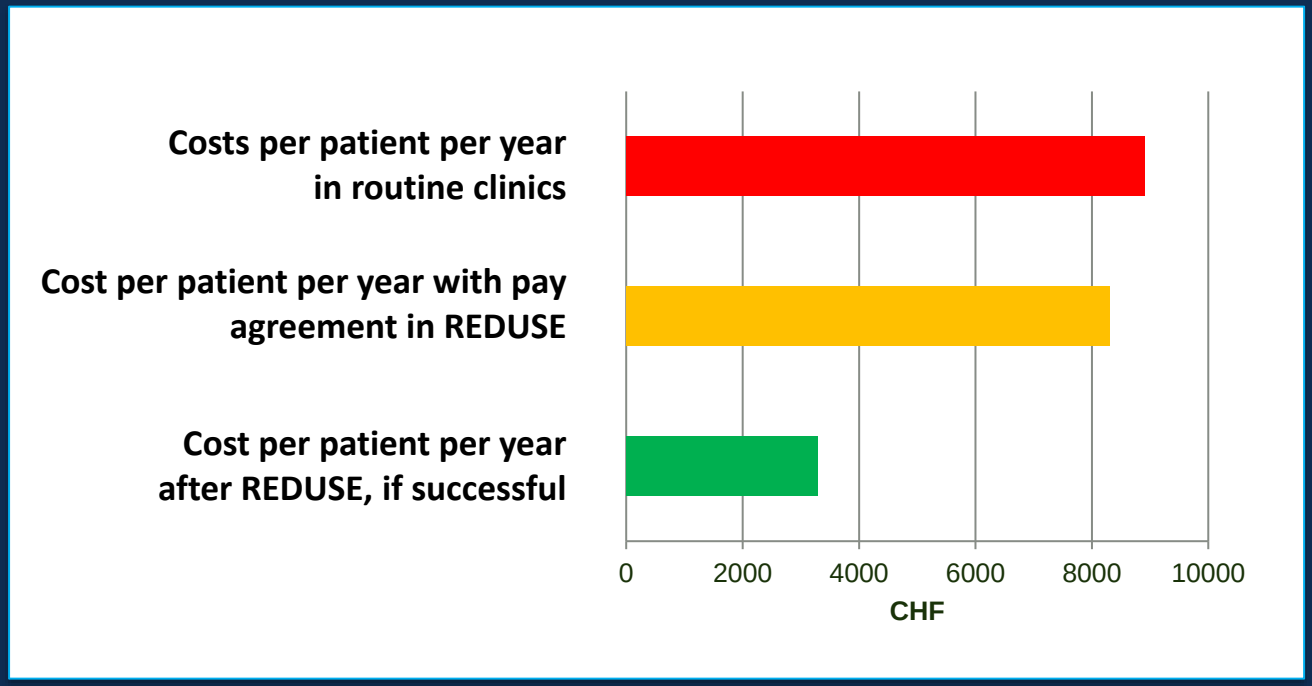
- **Primary objective**
  - To determine whether **120 mg** Denosumab every **12** weeks is **non-inferior** to **120 mg** every **4** weeks

- **Primary endpoint**
  - Time to first on-trial symptomatic skeletal event (SSE)

Presented by: Silke Gillessen

Funding

Sponsored in part by an umbrella organization of Swiss health insurance companies (Santésuisse)



Courtesy SAKK, R. von Moos

Presented by: Silke Gillessen

Benefits for Insurers

- Financing the trial is cost-neutral
- Potential cost reductions if the trial will show non-inferiority
- Less toxicity is associated with reduced secondary costs
- Develop track-record for supporting modern, patient-friendly trials

Presented by: Silke Gillessen

Important clinical questions in a rare situation of a rare cancer answered by a global collaboration

EORTC-GUCG
Study **1407**

A randomized phase lll trial of TIP vs TI-CE as initial salvage chemotherapy for patients with GCT

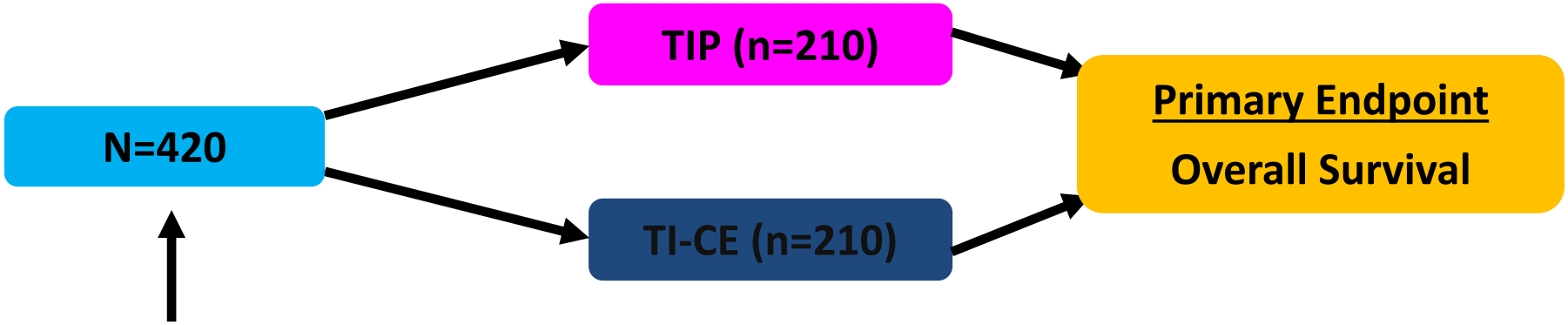
TIGER

PI: Darren Feldman, MD
Alliance GU Chair: Michael Morris, MD
ECOG PI: David Vaughn, MD
SWOG PI: David Quinn, MD
COG PI: Lindsay Frasier, MD
EORTC PI: Thomas Powles, MD, responsible EORTC GUCG: Silke Gillessen
Endorsed by SWOG, ECOG, EORTC, ANZUP

EORTC

The future of cancer therapy

Alliance A031102 (TIGER) Study design



Stratification:

- IPFSG risk class
- Continent

81% power to distinguish a 29% improvement in OS (HR of 0.71)

Secondary Endpoints

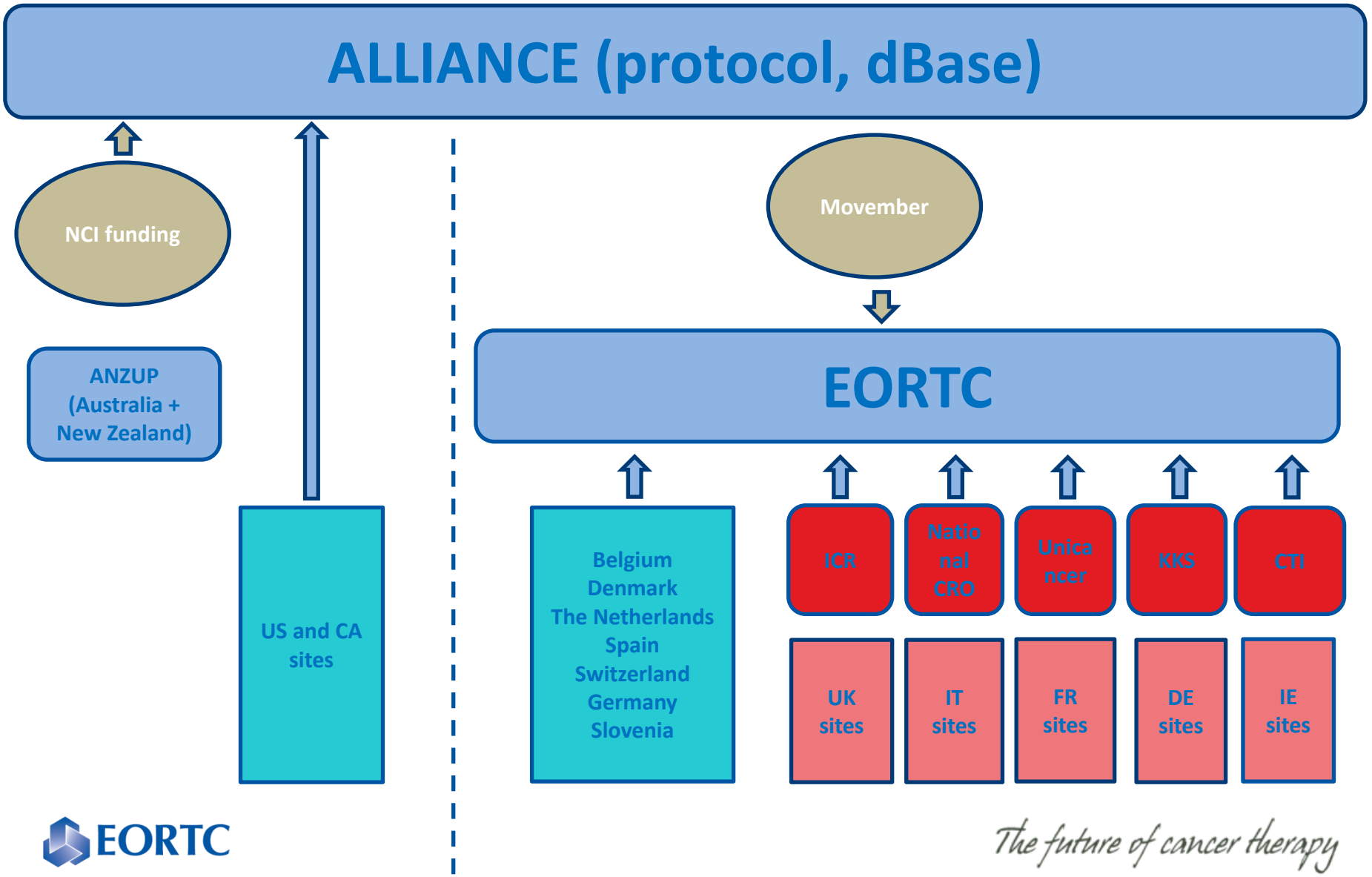
- PFS
- Favorable RR (CR / PR-m)
- Toxicity & treatment-related mortality
- Validation of IPFSG model
- Biological correlates (SNP & whole exome analyses)

PR-m = PR with normal tumor markers

IPFSG = International Prognostic Factors Study Group

EORTC

A Global Collaboration



EORTC

The future of cancer therapy

Summary: Academic groups are important for

- Development of new trial designs (MAMS, near equivalence…)

- Answer important clinical questions that are of no interest for pharmaceutical companies (de-escalation trials; «old drug» trials…)

Main question: How can we make international collaboration of academic groups easier?

- Can we do them with less burocracy?

- Can we perform the same protocol in different countries/groups and share the data?


grazie
mille