International collaboration on a very rare cancer: Adrenocortical Carcinoma

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CONSENSUS MEETING AND CONFERENCE
Improving the Methodology of Clinical Research on Rare Cancers Hotel Bedford Brussels, February 10th 2012

ADRENOCORTICAL CANCER EPIDEMIOLOGY

- **Incidence: 0.5-2 cases per million population per year**
- **Women are more often affected than men (ratio: 1.5)**
- **Age distribution: bimodal with a first peak in childhood and a second higher peak in the fourth and fifth decade**
- **An exceptionally high annual incidence has been reported for children in Southern Brazil**

Endocrine-Related Cancer (2005) **12** 667–680

Management of patients with adrenal cancer: recommendations of an international consensus conference

D E Schteingart, G M Doherty[1], P G Gauger[1], T J Giordano[2], G D Hammer, M Korobkin[3] and F P Worden

Ann Arbor 2003

Recommendations mainly based on expert opinion
Evidence level of available data very low

European ACC core Group Study


Hammer G
Ann Arbor
Fojo T
Bethesda
Seattle
Washington
Olympia
Spokane
Portland
Vancouver
Salem
Oregon
Idaho
Boise
Montana
Helena
North Dakota
Bismarck
Minnesota
Lake Superior
Maine
Augusta
New Hampshire
Vermont
Montpelier
New York
Concord
South Dakota
Pierre
Minneapolis
St. Paul
Wisconsin
Michigan
Lake Michigan
Lake Huron
Lake Ontario
Albany
Rochester
Buffalo
Wyoming
Salt Lake City
Milwaukee
Madison
Lansing
Detroit
Lake Erie
Hartford
Pennsylvania
New York
New Jersey
Trenton
Carson City
Sacramento
San Francisco
Nevada
Utah
Cheyenne
Nebraska
Omaha
Iowa
Ames
Chicago
Ann Arbor
Cleveland
Harrisburg
Pittsburgh
Philadelphia
Wilmington
Dover
Delaware
Annapolis
Maryland
Boulder
Denver
Colorado
Lincoln
Des Moines
Columbus
Ohio
Baltimore
Springfield
Illinois
Indianapolis
Indiana
Cincinnati
Ohio
Washington D.C.
Topeka
Kansas City
Kansas
Jefferson City
St. Louis
Louisville
Frankfort
Charleston
West Virginia
Virginia
Richmond
Norfolk
California
Colorado
Missouri
Kentucky
Los Angeles
San Diego
Arizona
Phoenix
Santa Fe
New Mexico
Oklahoma
Oklahoma City
Nashville
Tennessee
Greensboro
Raleigh
North Carolina
Charlotte
Little Rock
Memphis
Columbia
South Carolina
Atlanta
Arkansas
Birmingham
Alabama
Georgia
Montgomery
Dallas
Louisiana
Jackson
Mississippi
Texas
Austin
Baton Rouge
New Orleans
Houston
San Antonio
Rio Grande
Tallahassee
Jacksonville
Orlando
Tampa
Florida
West Palm Beach
Miami

Chemotherapy: prospective trials including more than 10 patients

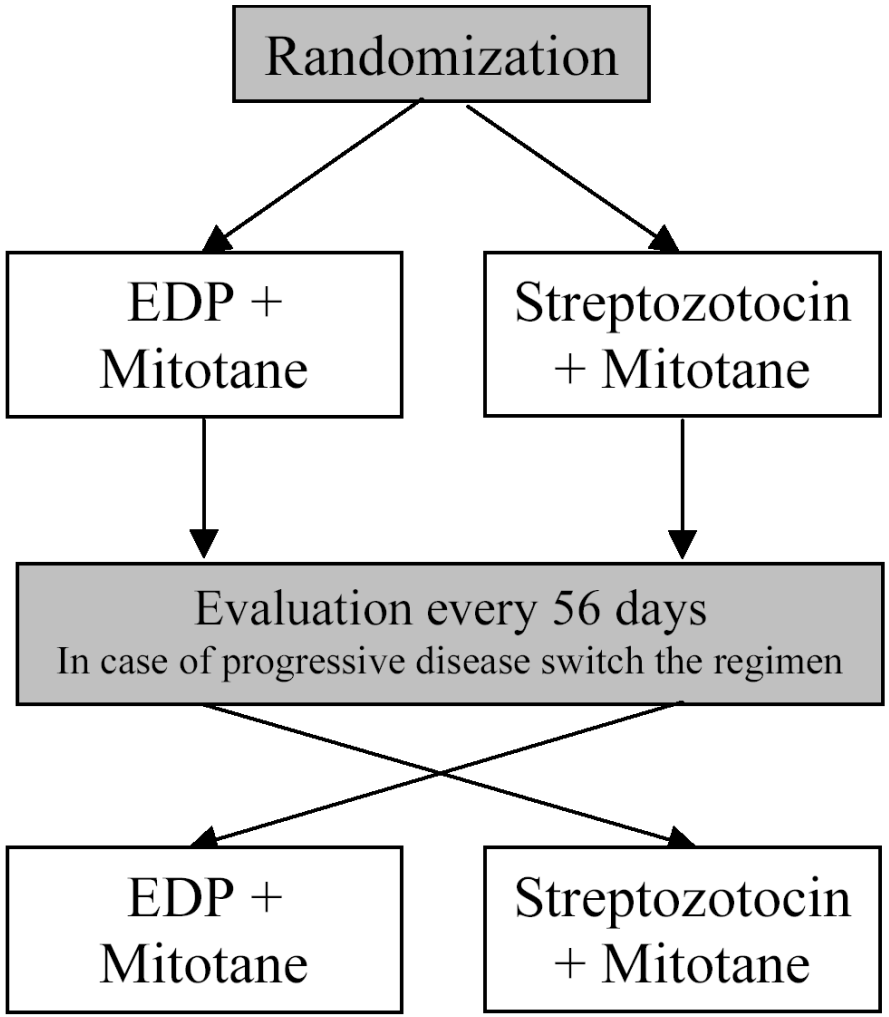
Author	Drugs	Pts	(CR+PR)
	CHEMOTHERAPY ALONE		
Van Slooten, 83	CDDP + DOXO + CTX	11	18%
Decker, 91	DOXO	16	19%
Schlumberger, 91	CDDP + DOXO + 5FU	13	23%
Burgess, 93	CDDP + VP16	13	46%
Williamson, 00	CDDP + VP16	45	11%
Total		98	18%
	CHEMOTHERAPY + MITOTANE		
Bonacci, 98	CDDP + VP16 + MIT (3-9 g/d)	18	33%
Khan, 00	STZ + MIT (1-4 g/d)	22	36%
Abraham, 02	VP16 + DOXO + VCR + MIT (6 g/d)	36	22%
Berruti, 05	CDDP + DOXO + VP16 + MIT (1-4 g/d)	72	49%
Total		148	42%

firm act study

An academic intention to treat study

Design:

- randomized
- prospective
- controlled
- open-label
- multi-center
- international
- parallel-group
- phase III trial



Second line therapy
as phase II trial

Recruting, follow-up, analysis
60+28+6 months = 7 years

FIRM-ACT Recruitment per country

	A	AUS	CAN	GER	F	Italy	NL	N	PL	SWE	US	**Total**
Population in million	8	28	33	82	64	60	16	5	38	9	311	
centers (n)	1	1	1	11	9	4	3	2	1	4	2	39
patients (n)	1	3	9	103	71	35	28	5	6	26	17	**304**

Patients are randomized from June 12, 2004 until Sept 17, 2009

Etoposide, doxorubicin, cisplatin, and mitotane versus streptozotocin and mitotane for advanced adrenocortical carcinoma – The FIRM-ACT study –

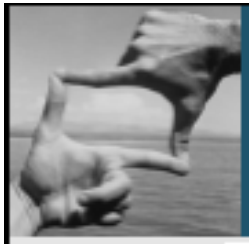
Martin Fassnacht, Massimo Terzolo, Bruno Allolio, Eric Baudin, Harm Haak, Alfredo Berruti, Staffan Welin, Carmen Schade-Brittinger, André Lacroix, Barbara Jarzab, Halfdan Sorbye, David J. Torpy, Vincenz Stepan, Wiebke Arlt, David Schteingart, Matthias Kroiss, Sophie Leboulleux, Paola Sperone, Anders Sundin, Ilse Hermsen, Stefanie Hahner, Holger S. Willenberg, Antoine Tabarin, Marcus Quinkler, C de la Fouchardière, Martin Schlumberger, Franco Mantero, Dirk Weismann, Felix Beuschlein, Hans Gelderblom, Hanneke Wilmink, Monica Sender, Maureen Edgerly, Werner Kenn, Tito Fojo, Hans-Helge Mueller, Britt Skogseid, for the FIRM-ACT study group

Submitted for publication

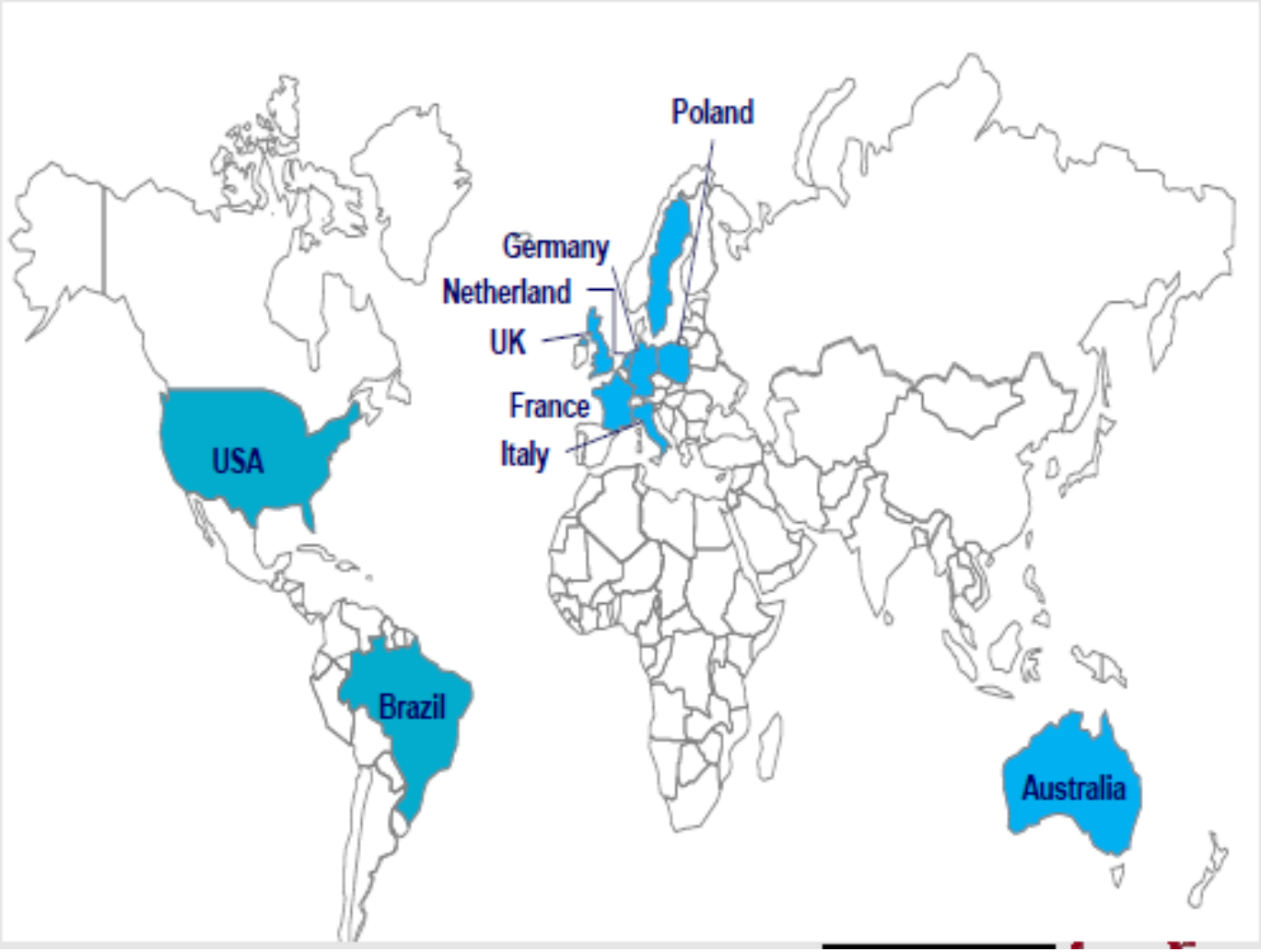
GALACCTIC TRIAL

OSI-906-301
A Randomized, Double-blind, Placebo-controlled, Phase 3 Study of OSI-906 in Patients with Locally Advanced or Metastatic Adrenocortical Carcinoma - Protocol Review

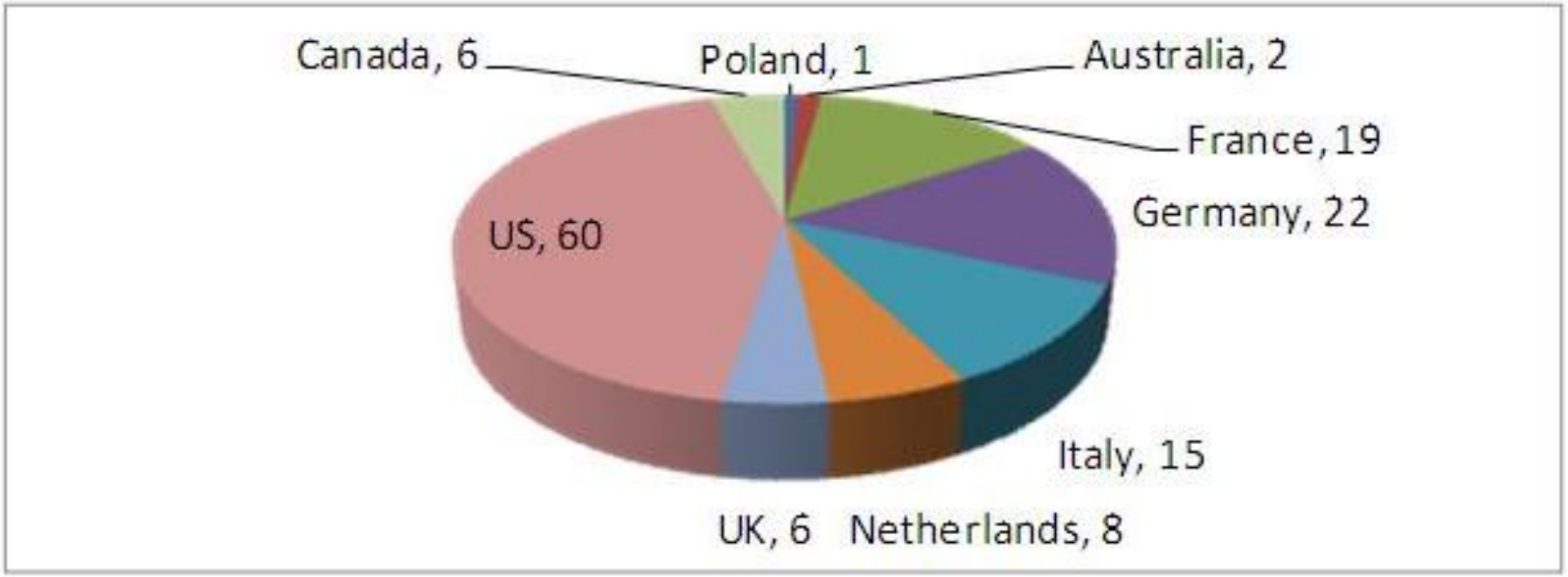
- Primary
  - To determine overall survival of single agent OSI-906 (Arm A) versus placebo (Arm B) in patients with ACC who received at least 1 but no more than 2 prior drug regimens



OSI 906-301: Countries



OSI 906 trial accrual completed: 139 Patients Randomized



Time lines of randomized studies in ACC

Firm-act accrual

Start 24/04/2004
End 02/10/2009

304 patients enrolled

GALACCTIC trial accrual

Start 15/02/2010
End 22/06/2011

139 patients enrolled

Adrenal Cancer Research Strategy

ENS@T ⟷ EORTC

Conclusion

A multinational cooperation makes feasible prospective randomized clinical trials in ACC

Each participating center increases its expertize and the number of patients referenced