

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

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**Investigators/Collaborators:**

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# Malignant ovarian germ cell tumor (MOGCT)

- Rare ovarian malignancy
  - 2-3% of all ovarian cancer
- Disease of children, adolescents, and young women
- 70% of MOGCT are early stage disease
- Highly curable due to high chemosensitivity
- Standard management
  - Fertility-sparing, complete staging or debulking surgery
  - Adjuvant BEP chemotherapy

# Treatment of FIGO Stage I MOGCT

- Treatment guidelines were adopted based on experiences of treating malignant testicular germ cell tumor
- Fertility-sparing, complete staging surgery
- **Adjuvant BEP chemotherapy**
  - Except *stage IA dysgerminoma* & *stage IA G1 immature teratoma*

# Surgery alone and surveillance strategy

- **Stage I malignant testicular germ cell tumors**
  - **75% of cases are cured by surgery alone**
  - **Most cases of recurrent disease were salvaged by chemotherapy**
  - **Overall survival is not compromised**
  - **75% of stage I disease can avoid futile chemotherapy**
  - **Surgery alone and surveillance strategy has been accepted as standard management for all stage I testicular germ cell tumors**

1. Kollmannsberger C et al. *Ann Oncol* 2010;21:1296-301
2. Schlatter M et al. *J Pediatr Surg* 2003;38:319-24

# BEP chemotherapy

- **Grade 3-4 neutropenia: 25%**
- **Febrile neutropenia: 10%**
- **Bleomycin-induced pulmonary complication: 10%**
  - **Sometimes fatal**
- **Cisplatin-induced renal impairment: 11-26%**
- **Cisplatin-induced ototoxicity**
- **Increased risk of cardiovascular disease**
- **Increased risk of secondary solid and hematologic malignancies**

1. Gershenson DM et al. *J Clin Oncol* 1990;8:715-20
2. Williams S et al. *J Clin Oncol* 1994;12:701-6
3. Fossa SD et al. *Ann Oncol* 2002;13:222-8
4. Lauritsen J et al. *Ann Oncol* 2015;26:173-8
5. Osanto S et al. *J Clin Oncol* 1992;10:574-9
6. Van den Belt-Dusebout AW et al. *J Clin Oncol* 2006;24:467-75
7. Travis LB et al. *J Natl Cancer Inst* 2010;102:1114-30

# Surgery alone and surveillance strategy in stage I MOGCT

Author	Year	Journal	N	Histology	Outcomes
Marina NM et al.	1999	JCO	44	IT	1 recur 1 salvaged 3Yr DFS:97.8%
Cushing B et al.	1999	AJOG	44	IT or YST	1 recur 1 salvaged
Baranzelli MC et al.	2000	EJC	12	MOGCT	6 recur 5 salvaged
Mann JR et al.	2000	JCO	9	MOGCT	3 recur 3 salvaged
Patterson DM et al.	2008	IJGC	35	MOGCT	11 recur 9 salvaged
Manglili G et al.	2010	GO	19	IT	2 recur 2 salvaged
Billmire DF et al.	2014	JCO	25	MOGCT	12 recur 11 salvaged 4yr DFS: 52% 4yr OS: 96%
			188		36 recur (19%) 32 salvaged (89%)

# Recent Clinical Trial

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ORIGINAL REPORT

## Surveillance After Initial Surgery for Pediatric and Adolescent Girls With Stage I Ovarian Germ Cell Tumors: Report From the Children's Oncology Group

*Deborah F. Billmire, John W. Cullen, Frederick J. Rescorla, Mary Davis, Marc G. Schlatter, Thomas A. Olson, Marcio H. Malogolowkin, Farzana Pashankar, Doojduen Villaluna, Mark Krailo, Rachel A. Egler, Carlos Rodriguez-Galindo, and A. Lindsay Frazier*

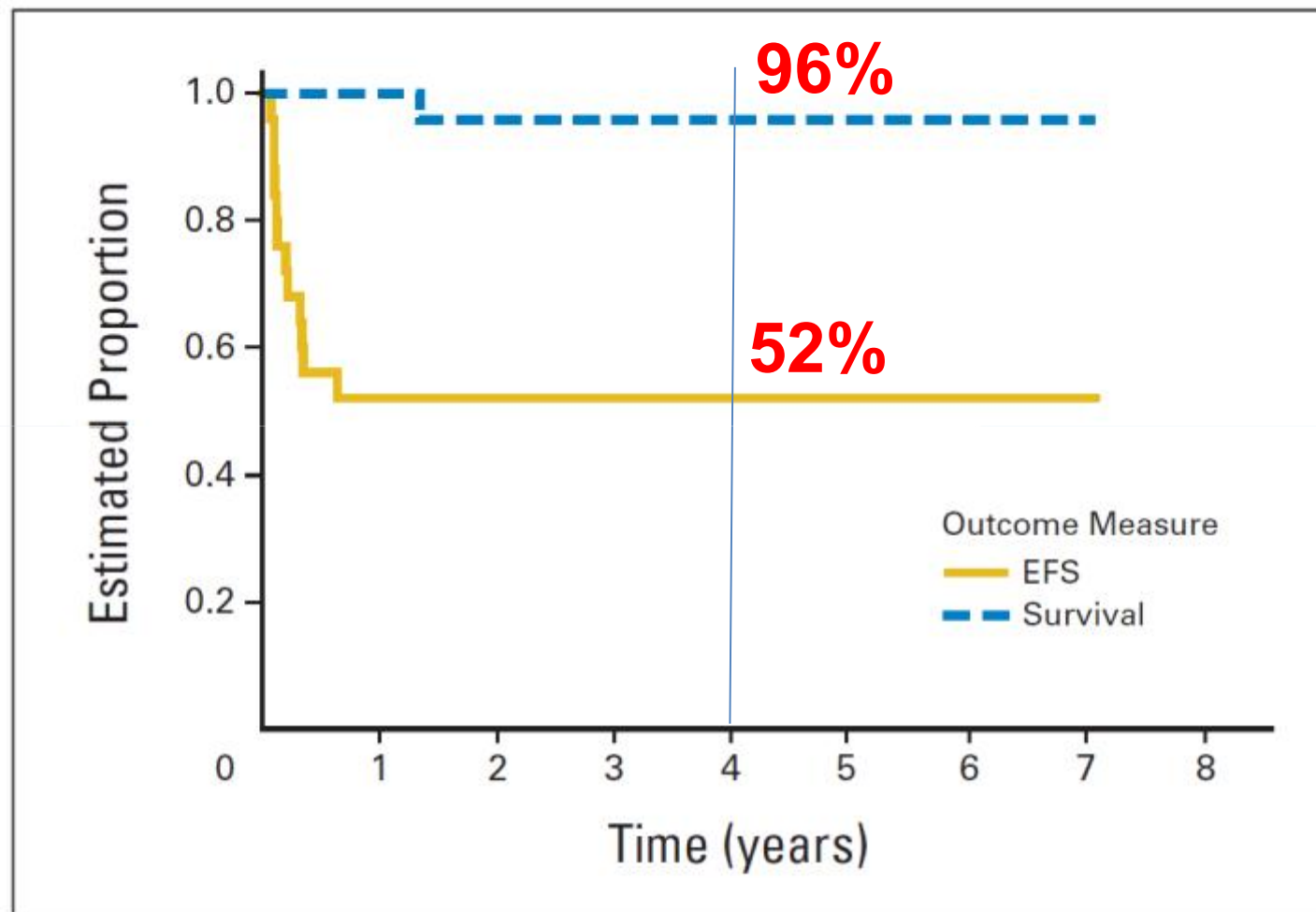
- Study period: 2003-2011
- Disease: Stage I MOGCT
- Age: 0-16 years (median, 12 years)
- Histology: YST, Embryomal Ca, ChorioCa, Mixed type
- 25 cases - YST: 11 / YST + IT (G2-3): 7 / Mixed: 7

# Recent Clinical Trial

- Surveillance
  - ~ 9 wks: tumor marker (aFP, bHCG) q 3 wks
  - 2-6 mos: tumor marker q 1 mos
  - 6-24 mos: tumor marker q 3 mos
  - Imaging study: not defined
- Persistence or recurrence
  - BEP 3 cycles
  - Bleomycin 15U/m<sup>2</sup> on day 1
  - Etoposide 167mg/m<sup>2</sup> on days 1-3
  - Cisplatin 33.3 mg/m<sup>2</sup> on days 1-3
  - 12 recurrences / 11 salvaged / 1 expired



# Recent Clinical Trial



**Fig 2.** Event-free survival (EFS) and overall survival of pediatric and adolescent female patients with stage I ovarian germ cell tumors.

# Recent Clinical Trial

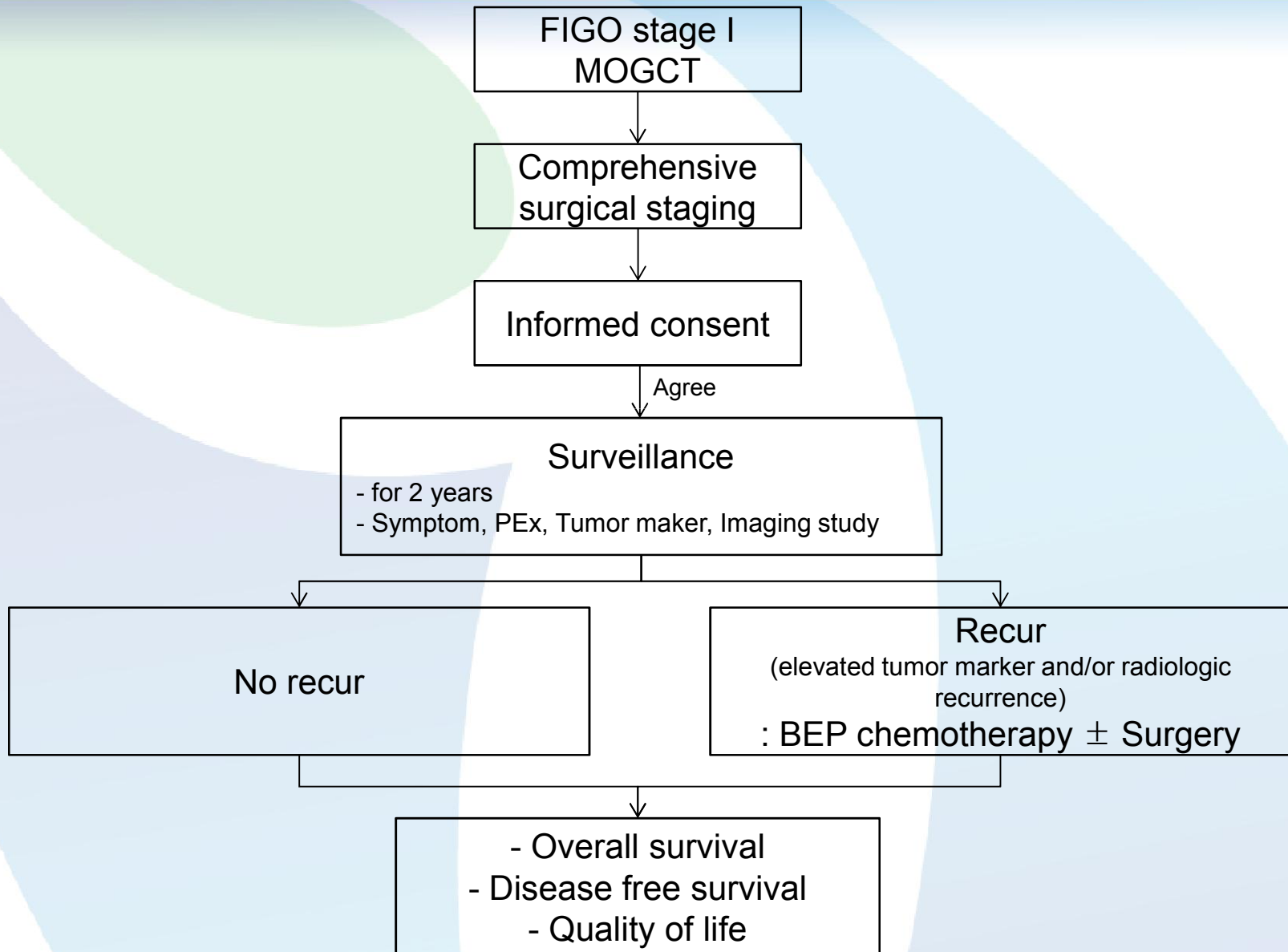
- Major limitation
  - Study included only children and young adolescent
  - Complete surgical staging was not defined.

# Summary

- Surgery alone and surveillance strategy in stage I MOGCT
  - 81% of cases can be cured by surgery alone
  - 89% of recurrent cases can be salvaged by chemotherapy and/or surgery
  - Overall survival is not compromised in surgery alone group
  - 81% of cases can avoid futile chemotherapy
- Further clinical trial is required
  - Including old adolescent and young adult
  - Complete surgical staging should be performed

# Study Scheme

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



# Eligibility

- Inclusion

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

- Exclusion

- Neoadjuvant chemotherapy
- Incomplete surgical staging
- FIGO stage II-IV

# Objectives

- **Primary objectives**
  - 3 year overall survival
- **Secondary objectives**
  - 3 year disease-free survival
  - Pattern of recurrence
  - Salvage rate at recurrence
  - Quality of life
  - Ovarian function
  - Treatment related complication

# Complete staging operation

- UO or USO
- Ovarian cystectomy for contralateral ovarian tumor
- Peritoneal exploration
- Peritoneal cytology
- Partial omentectomy
- Adhesiolysis and peritoneal biopsy
- LN evaluation: pelvic and paraaortic sampling or dissection

# Follow-up

- Tumor marker
  - Indicated if markers elevated at initial presentation
  - 3 mos: every mos
  - 3-24 mos: every 3 mos
- Radiologic imaging (Chest X-ray, CT, MRI)
  - Not indicated unless markers normal at initial presentation
  - 1 mos and 3 mos: imaging
  - ~24 mos: every 6 mos
- Physical examination
  - ~24 mos: every 3 mos



# Treatment at recurrence

- Surgery
  - Depending on the decision of surgeon
- BEP chemotherapy (no less than 3 cycles)
  - One of 2 regimen
  - 3 day regimen
    - Bleomycin  $15\text{U}/\text{m}^2$  on day 1
    - Etoposide  $167\text{mg}/\text{m}^2$  on days 1-3
    - Cisplatin  $33.3\text{ mg}/\text{m}^2$  on days 1-3
  - 5 day regimen
    - Bleomycin  $15\text{U}/\text{m}^2$  on day 1
    - Etoposide  $100\text{mg}/\text{m}^2$  on days 1-5
    - Cisplatin  $20\text{ mg}/\text{m}^2$  on days 1-5

# Study duration and patients number

- Study duration
  - 4 years
- Study patients
  - 100 case

# Study evaluation

- Overall survival
- Disease-free survival
- Treatment-related complication
- Quality of life
- Ovarian function

# Acknowledgements

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None.

**Thank you for your kind attention !!!**