Ovarian Cancer Patients Who Have Received Multiple Prior Therapies: When to Stop or Continue Treatment?

Eric Pujade-Lauraine, MD, PhD
Centre des Cancers de la Femme et Recherche Clinique
Centre Hospitalier Universitaire Hôtel-Dieu
Paris, France

What Does "Multiple Lines" Mean?

- **Multiple lines is at least 3 previous lines: a minimum of 1 front-line (including maintenance) and 2 lines of chemotherapy. Thus, from the 4th line of therapy**
- **In this setting, randomized trials are scarce, and prognostic factors relatively unknown**

Lines of Chemotherapy Criteria in Resistant/Refractory Randomized Trials

Trial	Line
Canfosfamide vs PLD or topotecan[1]	3rd
Patupilone vs PLD[2]	2nd to 4th
Bevacizumab + Cx vs Cx (AURELIA)[3]	2nd to 3rd
Pertuzumab + Cx vs Cx[4]	2nd to 3rd
Lurbinectedin vs topo[5]	2nd to 3rd

4th line = 6%

1. Vergote I, et al. *Eur J Cancer.* 2009;45(13):2324-2332; 2. Colombo N, et al. *J Clin Oncol.* 2012;30(31):3841-3847; 3. Pujade-Lauraine E, et al. *J Clin Oncol.* 2014;32(13):1302-1308; 4. AGO, on-going; 5. Poveda A, et al. *J Clin Oncol.* 2014;32(5S): Abstract 5505..

Multivariate Analysis of PFS at Each Relapse: An AGO-GINECO Analysis

PFS criteria, HR	2nd line n = 1552	3rd line n = 829	4th line n = 414	5th line n = 178
Age	1.01	1.01	1.00	1.00
ECOG 2 vs 0-1	1.15	1.27	0.78	1.00
FIGO IIIC-IV vs IB-IIIB	1.26	1.41	1.24	0.92
Grade 2-3 vs 1	1.13	1.74	1.49	0.16
Histology muc vs sero	0.98	1.21	1.08	3.04
Residue >0 vs 0 mm	1.34	1.52	1.21	0.79
Platinum-Sensitive vs Resistant	**0.64***	**0.68***	**0.80**	**1.02**

Hanker LC, et al. Ann Oncol. 2012;23(10);2605-2612.

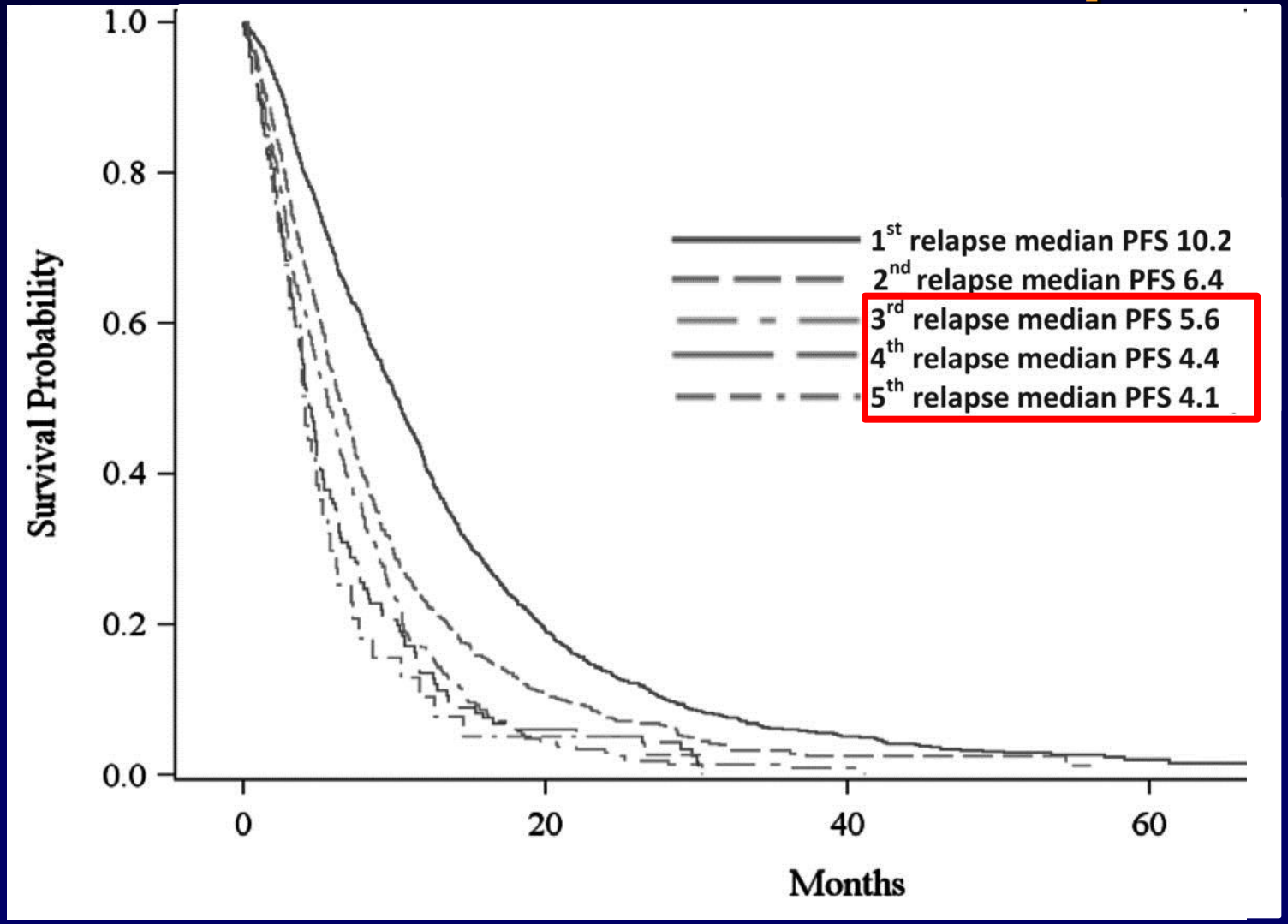
* $P<.05$

Platinum-Free Interval (PFI) in 4th Line

- PFI is <6 months in 33/40 pts (82%) having reached the 4th line of therapy
- Even patients having progressed under the last chemotherapy regimen have still a small chance to achieve an objective response (n = 2/20, ORR = 10%)

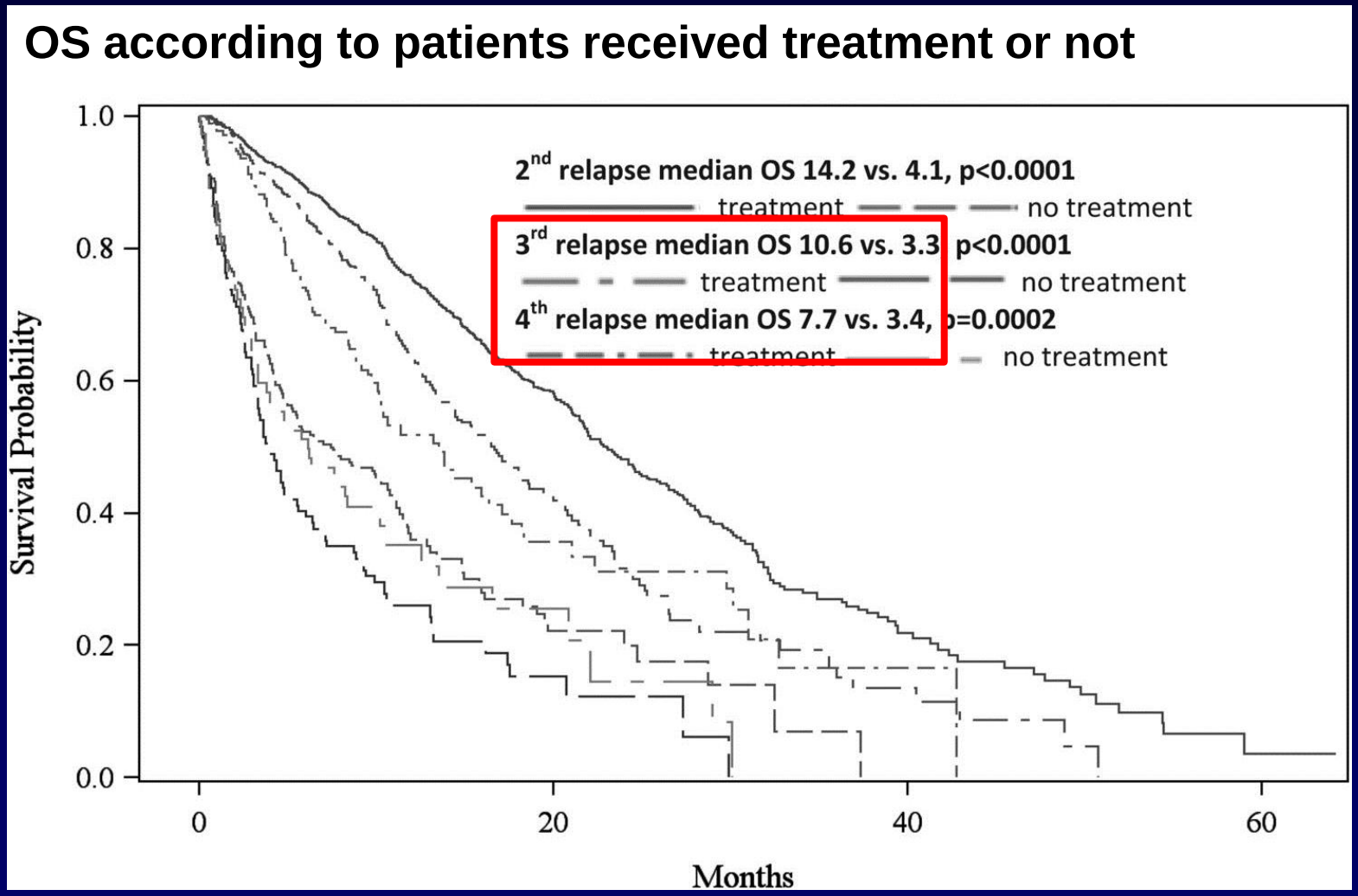
Pujade-Lauraine E, unpublished

Outcome After Multiple Lines Median PFS for Each Relapse



Hanker LC, et al. *Ann Oncol*. 2012;23(10);2605-2612.

To Treat or Not to Treat The Disease ?



Hanker LC, et al. *Ann Oncol*. 2012;23(10);2605-2612.

Treatment Outcome and Survival in Participants of Phase I Oncology Trials

n = 180 pts

Overall RR = 7.2%
Disease control rate = 48.2%

Italiano A, et al, *Ann Oncol.* 2008;19(4):787-792.

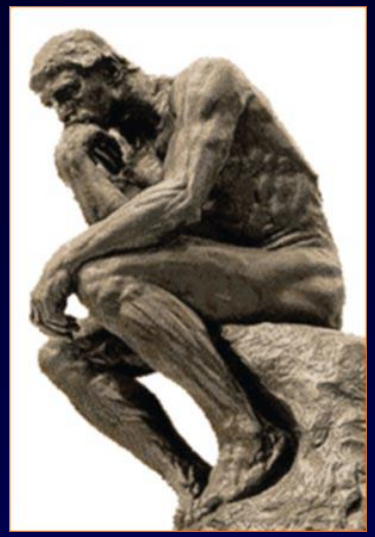
The Choice of Treatment: The Armamentarium

- Chemo single drugs approved: platinum, paclitaxel, PLD, gemcitabine, topotecan
- Chemo combination: platinum (carboplatin) + paclitaxel, PLD, gemcitabine; trabectedin + PLD
- Biologic therapy approved: bevacizumab, olaparib (BRCA+)

The Choice of Treatment: The Armamentarium (cont)

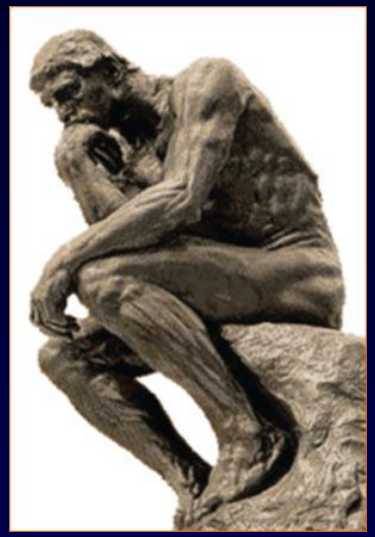
- Surgery
- Hormonotherapy
- Other active single drugs: cyclophosphamide, hexamethylmelamine, docetaxel, pemetrexed, etoposide, etc…
- Other biologic therapy: trastuzumab (HER2), everolimus (m-TOR pathway), vemurafenib (BRAF), anti-MEK (ERK/MEK pathway)

If You Are Fond of Aphorisms!



Don’t hurry to treat when CA125 level increases

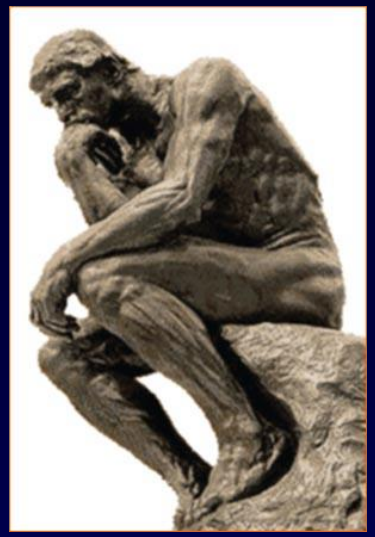
A drug that has failed has a low chance to succeed

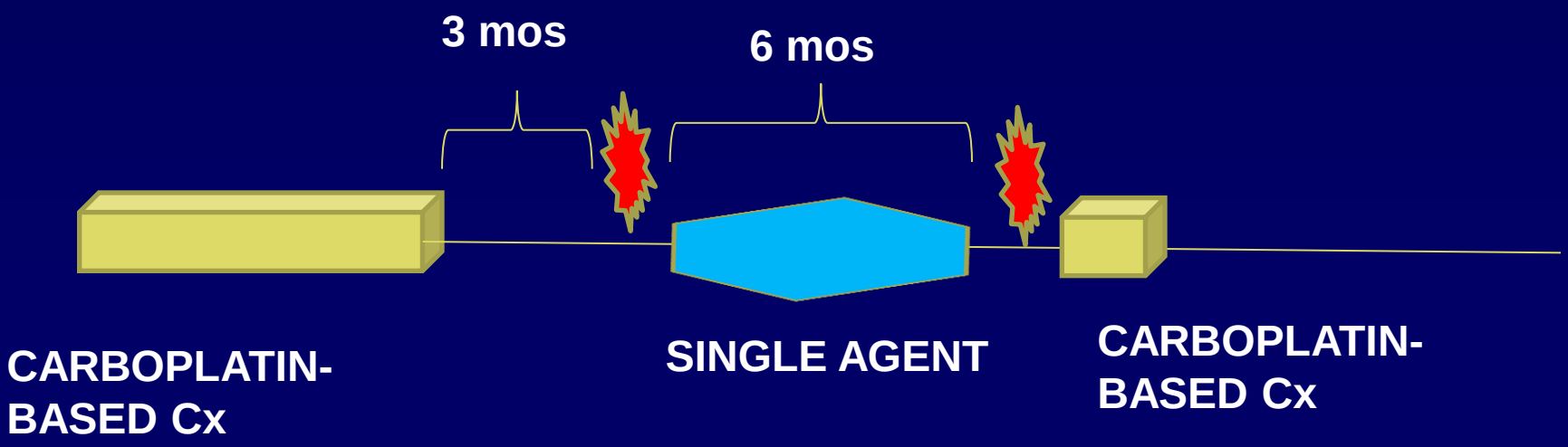


- **Except PACLITAXEL!**

  One of the best drugs for q3 wk paclitaxel-resistant disease is weekly paclitaxel

When platinum-free interval is over 6 months, try platinum again

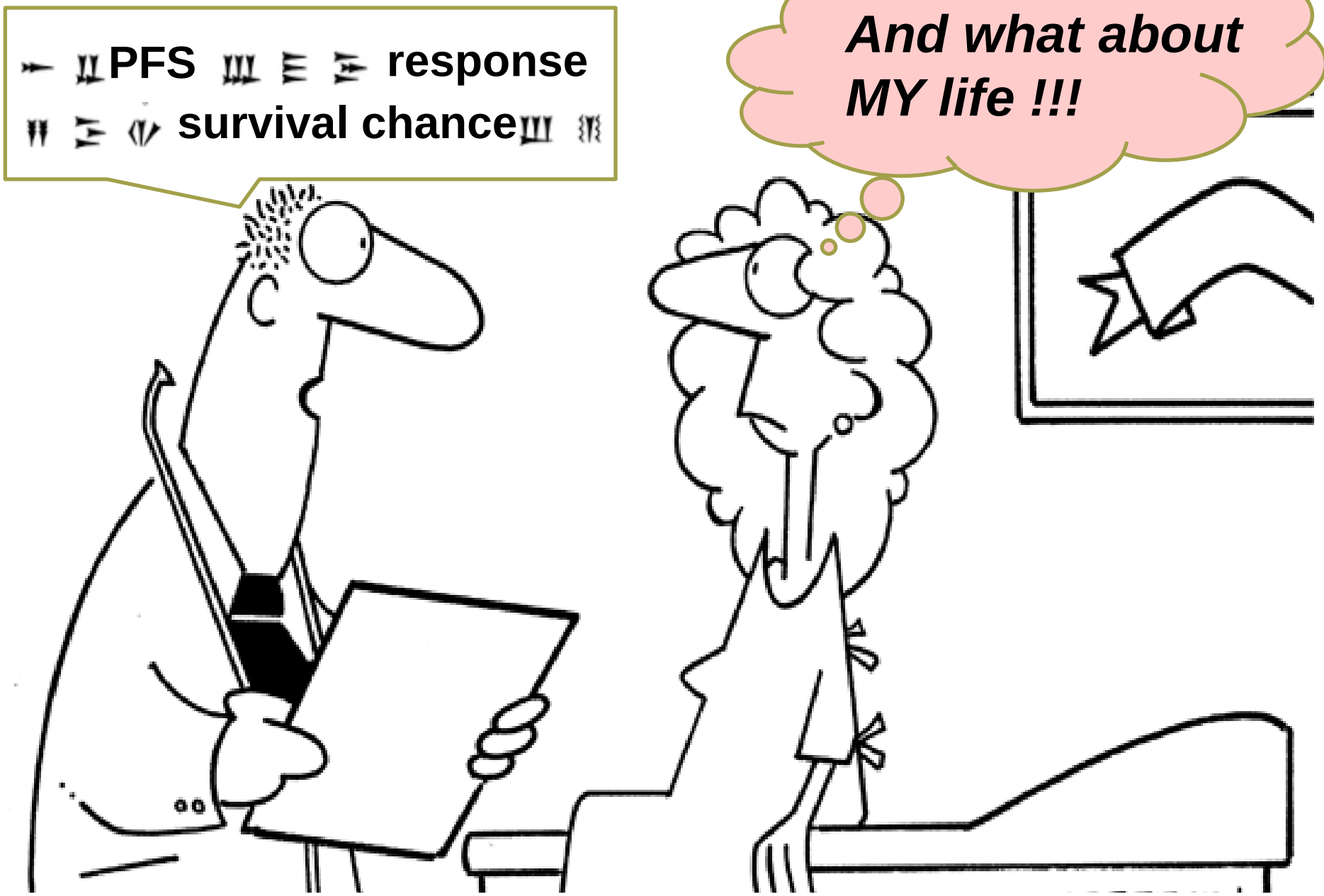




Choice Not to Treat the Disease

- Poor response rate and outcome
- Toxicity of anticancer treatments

= palliative care is the best option


PFS response
survival chance
And what about MY life !!!

Would you like to listen to ME!!! I need you

“What do you believe is the most effective in regards to informing you about the various possibilities of therapy available?”

1. **A talk with the treating doctor** **85%**
2. **Information offered on the internet** **12%**

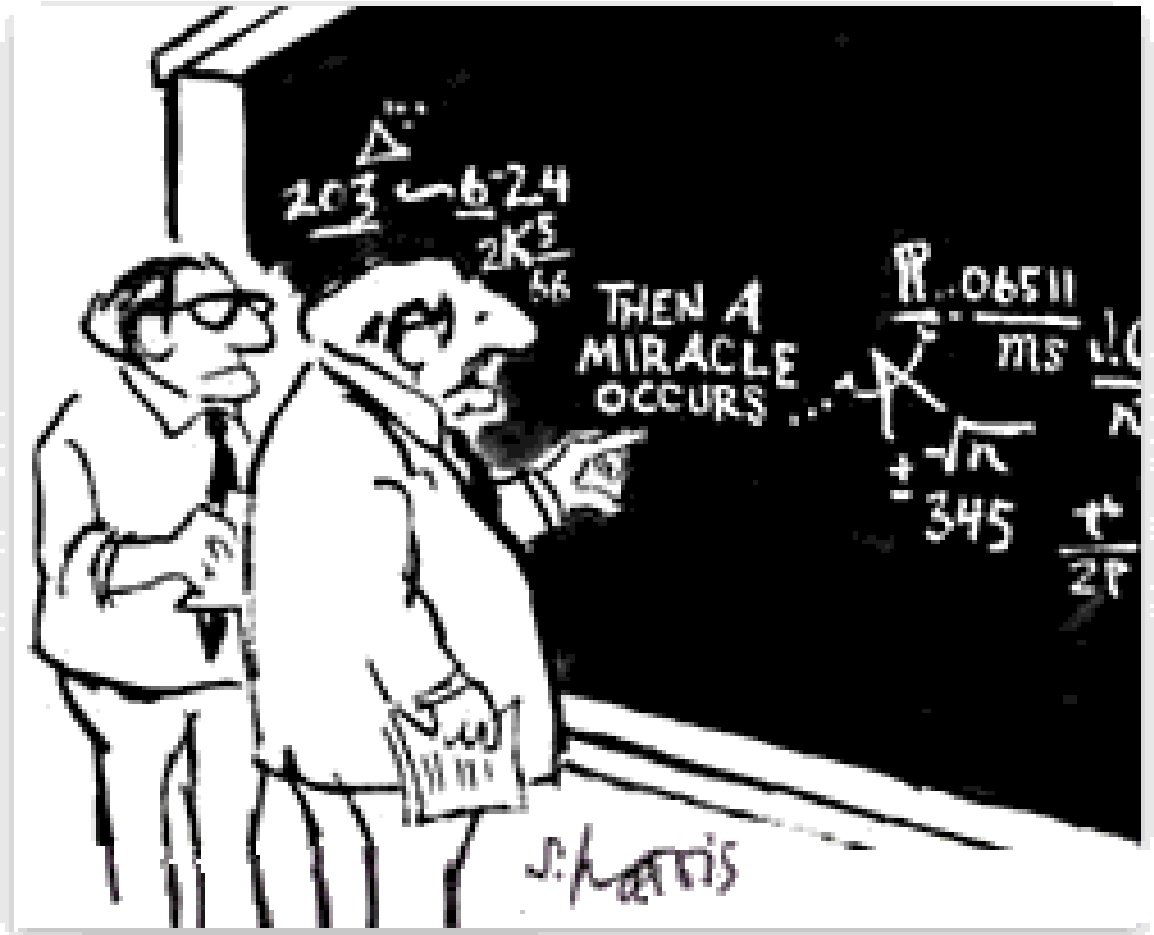
Oskay-Özcelik g, et al. *J Clin Oncol,* 2013;31(Suppl): Abstract 5569.

Listen to my hopes

I am hoping

1. Just for a less painful course of sickness	6%
2. For no recurrence of tumor-related symptoms	35%
3. To live longer than I otherwise would	24%
4. For complete healing without any further complications	28%

Oskay-Özcelik G, et al. *J Clin Oncol,* 2013;31(Suppl): Abstract 5569.



"I THINK YOU SHOULD BE MORE EXPLICIT HERE IN STEP TWO."

Olaparib Trial in Heavily Pretreated Ovarian Cancer

- n = 137 pts with measurable disease, g*BRCA*+, and treated with at least 3 lines of prior therapy
- Response rate: 34% (26-42) with a median response duration of 7.9 months
- Conditional approval by FDA

Adjusting Hope With Reality

- **Disparity of expectation and perceived benefit from treatment is correlated with scores of depression**

Sjoquist KM, et al. *Oncologist*. 2013;18(11):1221-1228.

Listen to my desire

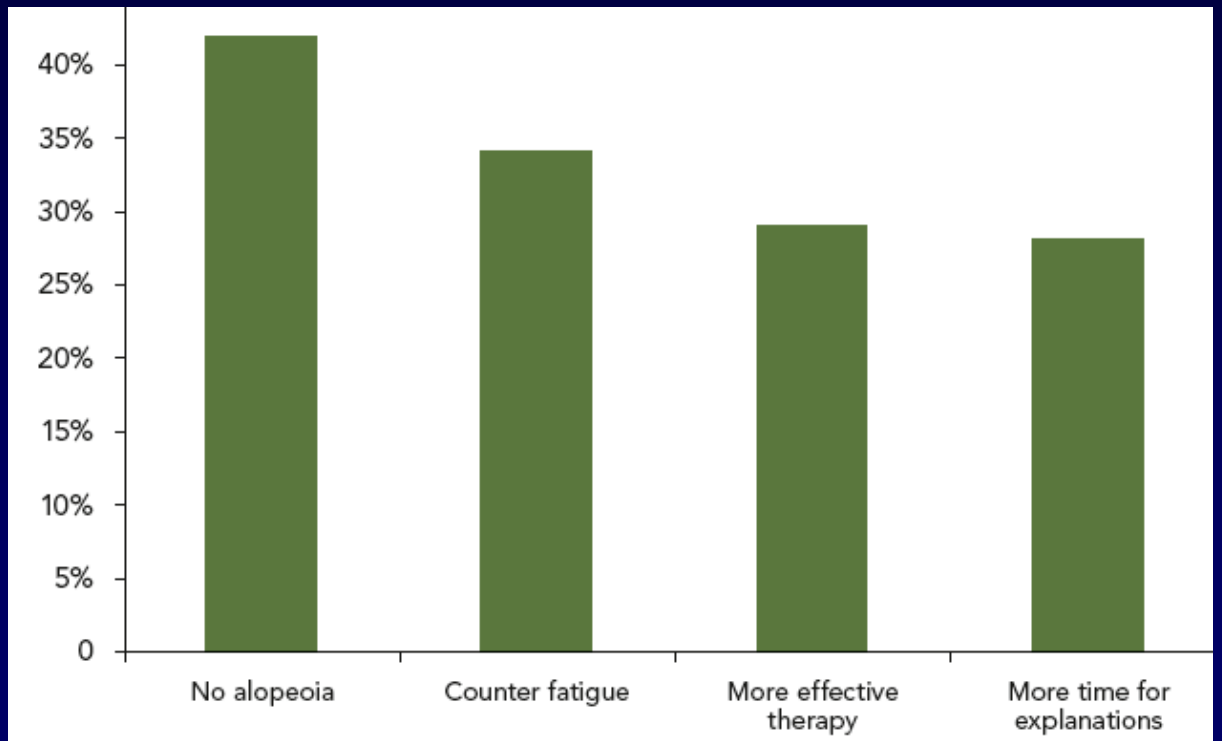


Figure 7: If there would be things you could do to improve the treatment of ovarian cancer, which of them would you say would be the most important?

Oskay-Özcelik G, et al. *J Clin Oncol,* 2013;31(Suppl): Abstract 5569.

Listen to my pain and relieve me!

Symptom	Total (% pts) n = 364
Fatigue	39.0
Trouble sleeping	30.2
Abdominal bloating	29.7
Abdominal pain	28.6
Pain	26.4
Constipation	23.6
Shortness of breath	23.1
Frequent urination	19.8
Lack of appetite	15.9
Satiety	14.8
Indigestion	15.4
Nausea	15.9
Vomiting	11.0
Diarrhea	15.4

From AURELIA study

Conclusion

- Taking care of a patient treated with multiple prior therapies: fruit of a personal dialogue assessing her needs, her symptoms, her fragility, her expectations, to find what is her best option

- It is the setting where merely applying standard regimens is of no more use.
  You need the essence of the medical art: Humanity

2015

Progress and Controversies in Gynecologic Oncology Conference