bjclub breast Journal Club

L'IMPORTANZA DELLA RICERCA IN ONCOLOGIA

20 - 21 APRILE
2023 ROMA

THE HIVE HOTEL

Via Torino, 6

THE OXFORD DEBATE EDITION

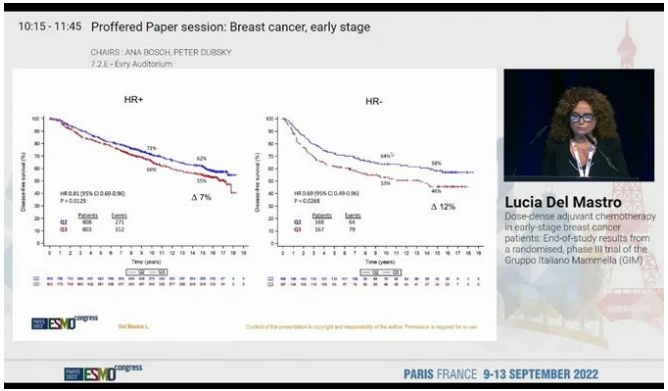
Disclosures

Consultancy/Advisory Board:

Daiichi Sankyo, AstraZeneca, Roche, Seagen, EISAI, Pfizer, Lilly, Novartis, Amgen, MSD, Chugai, Sanofi, Gilead, Exact Science, Agendia

Congratulations to Lucia, all co-authors GIM!

ESMO 2022



Fluorouracil and dose-dense adjuvant chemotherapy in patients with early-stage breast cancer (GIM2): end-of-study results from a randomised, phase 3 trial

*Lucia Del Mastro, Francesca Poggio, Eva Blondeaux, Sabino De Placido, Mario Giuliano, Valeria Forestieri, Michelino De Laurentiis, Adriano Gravina, Giancarlo Bisagni, Anita Rimanti, Anna Turletti, Cecilia Nisticò, Angela Vaccaro, Francesco Cognetti, Alessandra Fabi, Simona Gasparro, Ornella Garrone, Maria Grazia Alicicco, Ylenia Urracci, Mauro Mansutti, Paola Poletti, Pierpaolo Correale, Claudia Bighin, Fabio Puglisi, Filippo Montemurro, Giuseppe Colantuoni, Matteo Lambertini, Luca Boni, on behalf of the Gruppo Italiano Mammella Investigators**

Clinical research

Pharma

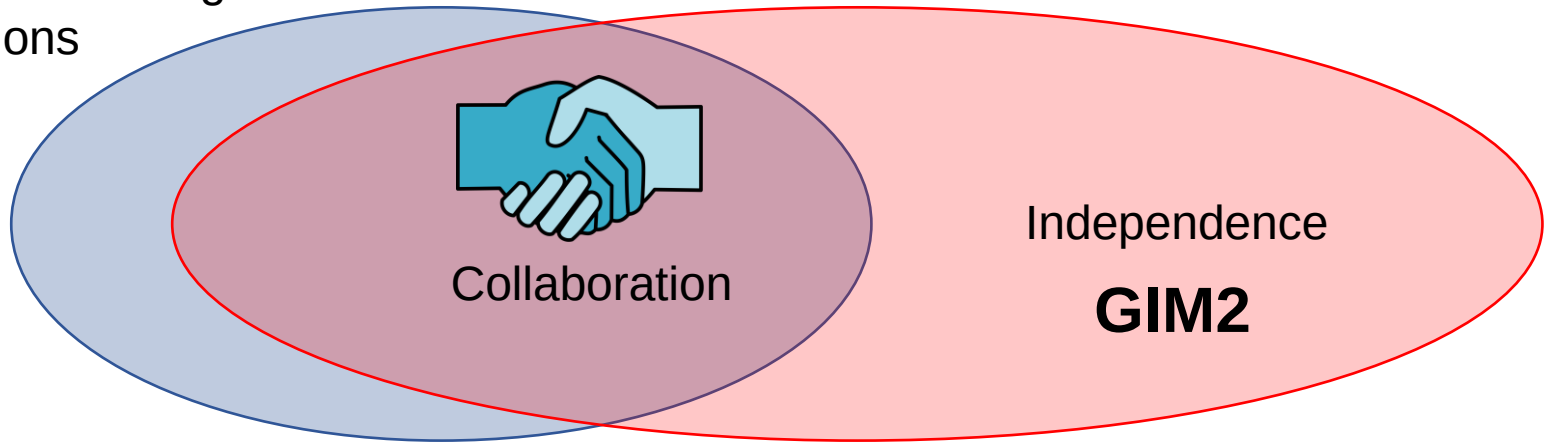
Academia

Clinical research

Pharma **Academia**

Clinical research questions

Clinical meaningless questions



GIM2: which clinical questions?

Does Fluorouracil matter?

Does dose-dense matter?

Are these questions clinically relevant?

YES

Best (neo)adjuvant chemotherapy regimen

What?

Anthracyclines
(epirubicin, doxorubicin)

Cyclophosphamide

Fluorouracil

Taxane
(paclitaxel, docetaxel)

Add on?

Pharma

Academia

Best (neo)adjuvant chemotherapy regimen

What?

Anthracyclines
(epirubicin, doxorubicin)

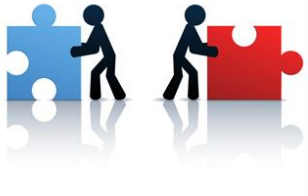
Cyclophosphamide

Fluorouracil

Taxane
(paclitaxel, docetaxel)

Take out?

Pharma



Accademia

Best (neo)adjuvant chemotherapy regimen

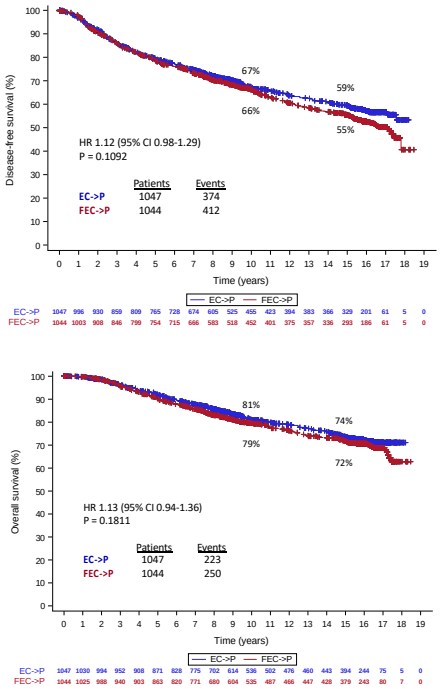
What?

Anthracyclines
(epirubicin, doxorubicin)

Cyclophosphamide

Fluo[redacted]racil

Taxane
(paclitaxel, docetaxel)



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Best (neo)adjuvant chemotherapy regimen

Academia

How?

Sequential vs Concomitant

Dose

Dose

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Dose escalation

Dose intensity

Total dose (duration)

Dose density

Rationale for “dose-dense”

VIEWPOINT
www.nature.com/clinicalpractice/onc

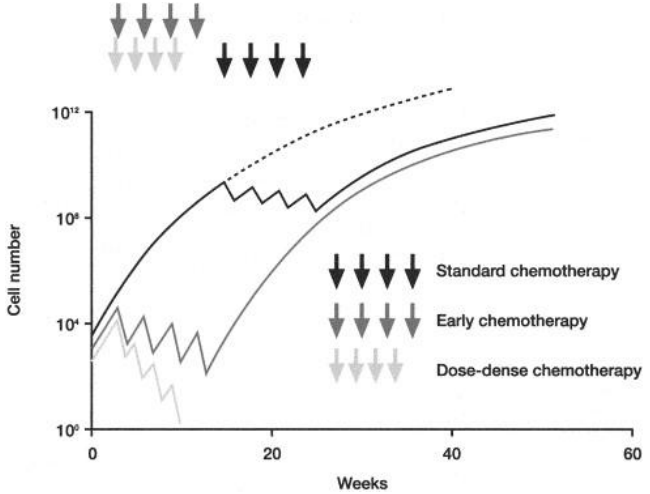
The Norton–Simon hypothesis: designing more effective and less toxic chemotherapeutic regimens

Richard Simon* and Larry Norton

R Simon is Chief of the Biometric Research Branch at the National Cancer Institute, Bethesda, MD, USA. L Norton is Deputy Physician-in-Chief of Memorial Hospital and Medical Director of the Evelyn H. Lauder Breast Center, Memorial Sloan-Kettering Cancer Center, New York, NY, USA.

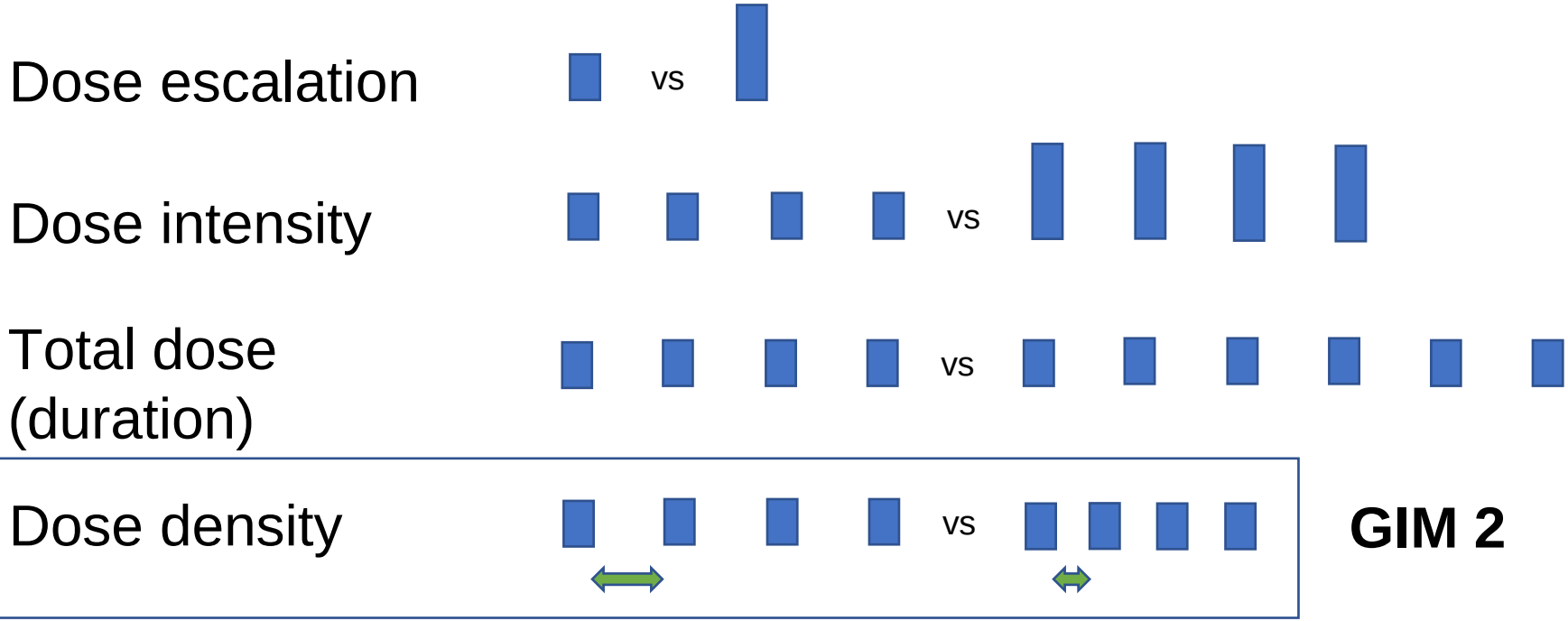
Successful treatment of bacterial infections is largely a result of our ability to exploit the biochemical differences between bacteria and human cells so as to achieve toxic drug concentrations in the former while sparing the latter. Unfortunately, such high selectivity is at present elusive in the chemotherapy of human cancers. Hence, great effort is required to determine dose schedules that maximize the benefit/toxicity ratio, particularly for multiple agent regimens.

Extensive clinical experience has taught us that trial-and-error, in the absence of guiding principles, is inefficient in this regard. Seeking guiding principles, we used clinical and laboratory observations to derive a phenomenological law relating the effect of cytotoxic chemotherapy on integrated drug effect, the chance of eradicating the tumor is maximized by delivering the most effective dose level of drug over as short a time as possible. Thereby, tumors given less time to grow between treatments are more likely to be eradicated. Administering high quantities of the drug at the beginning of the chemotherapy cycle (i.e. front-loading) might fail for two reasons. First, levels higher than a certain concentration may not increase the killing of cancer cells. Second, even if they did, the toxicity could be intolerable. In practice, optimizing the schedule means determining a way to give the maximum integrated effect over as short a time as possible, consistent with reasonable quality of life.



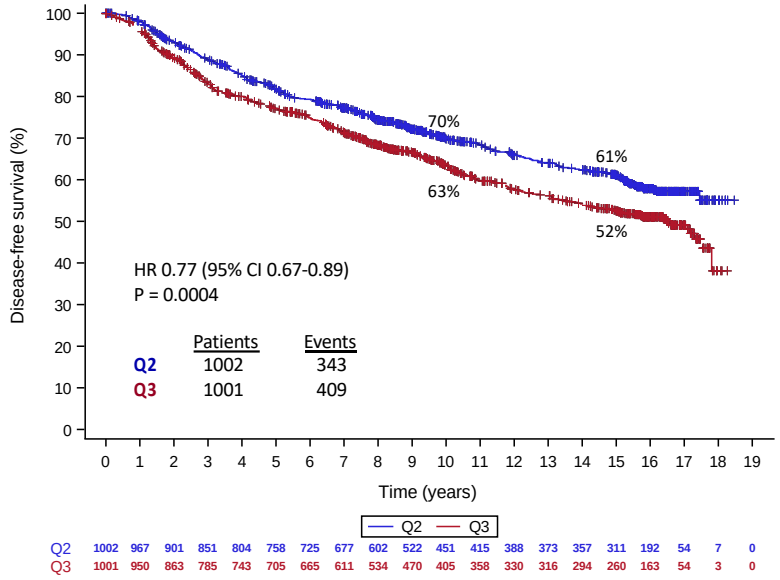
Optimizing dose

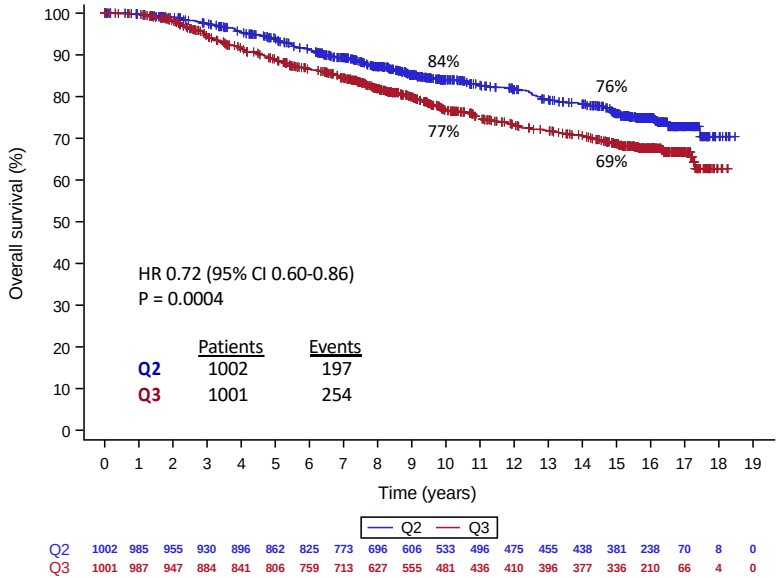
Academia



GIM 2

Dose-dense improve DFS and OS





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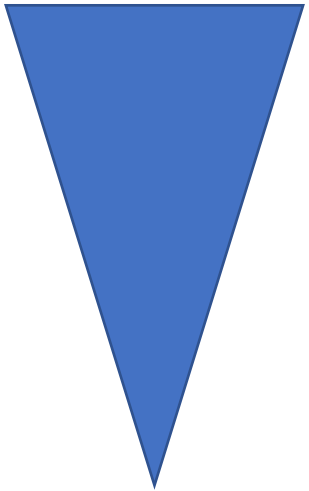
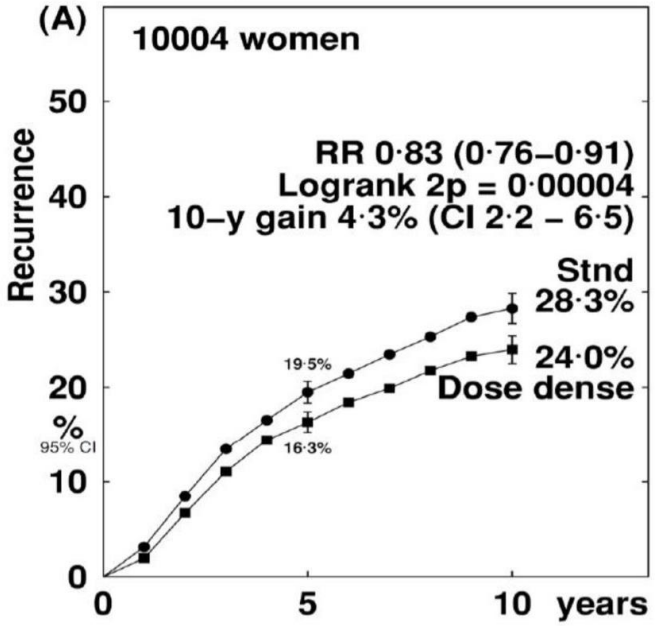
Dose-dense improve DFS and OS

Highest degree of clinical relevance

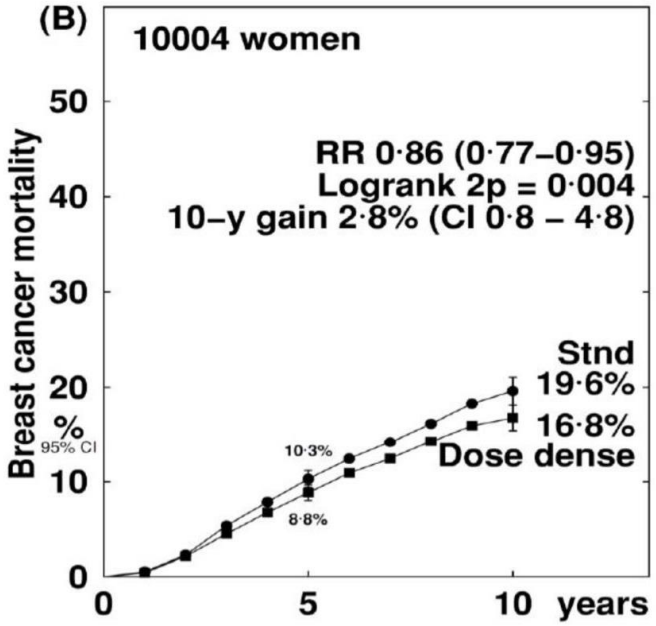


2-weekly (dose dense) *vs* the same chemotherapy given 3-weekly

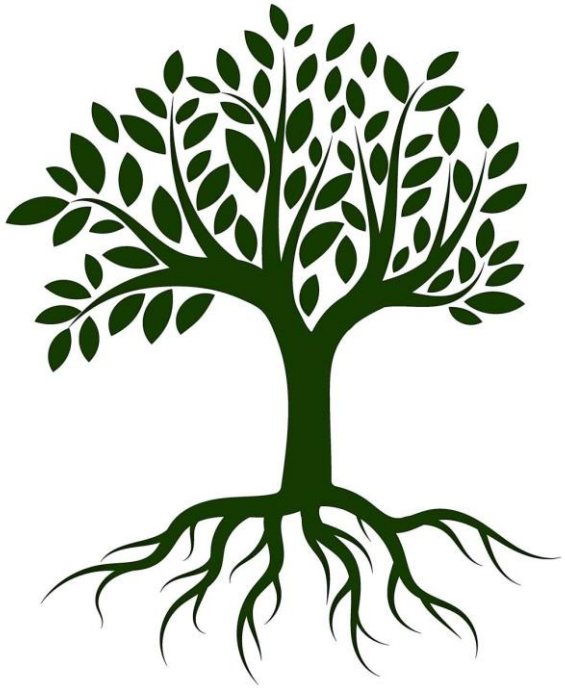
Any Recurrence



Breast Cancer Mortality



Key Italian contribution in cancer research



GIM 2

Gruppo Italiano Mammella GIM

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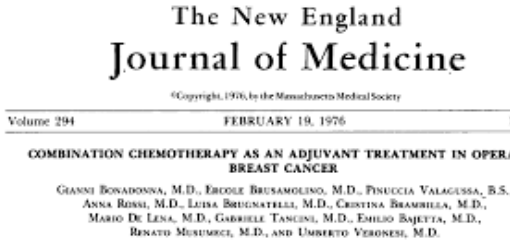


The New England
Journal of Medicine

Volume 294 FEBRUARY 19, 1976

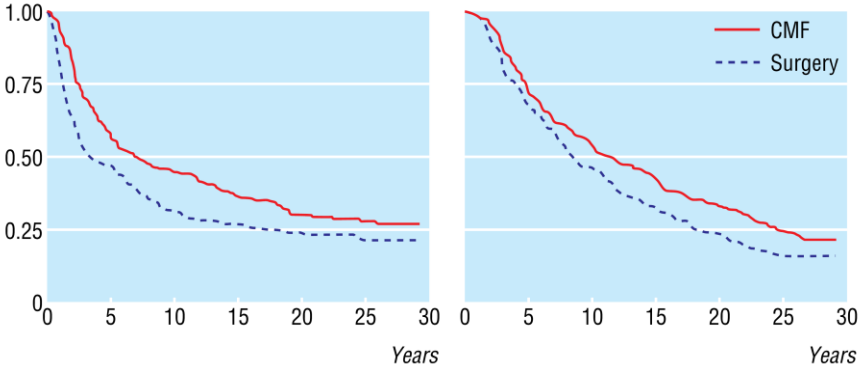
COMBINATION CHEMOTHERAPY AS AN ADJUVANT TREATMENT IN OPER BREAST CANCER

GIANNI BONADONNA, M.D., ERCOLE BRUSAMOLINO, M.D., PINUCCIA VALAGUSSA, B.S., ANNA ROSSI, M.D., LUISA BRUGNATELLI, M.D., CRISTINA BRAMBILLA, M.D., MARIO DE LENA, M.D., GABRIELE TANCINI, M.D., EMILIO BAJETTA, M.D., RENATO MUSUMECI, M.D., AND UMBERTO VERONESI, M.D.

Quality information provided only by academia: very long follow-up

30 years' follow up of randomised studies of adjuvant CMF in operable breast cancer: cohort study

Gianni Bonadonna, Angela Moliterni, Milvia Zambetti, Maria Grazia Daidone, Silvana Pilotti, Luca Gianni, Pinuccia Valagussa



Bonadonna G BMJ 2005

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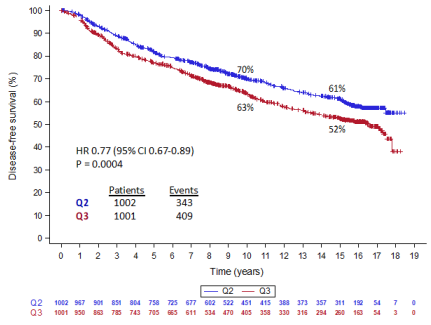

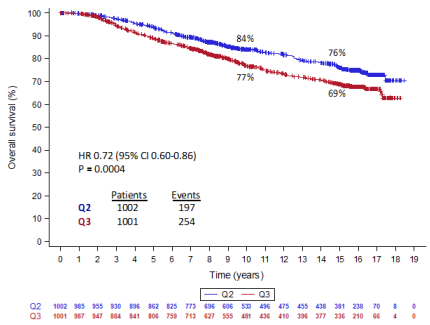

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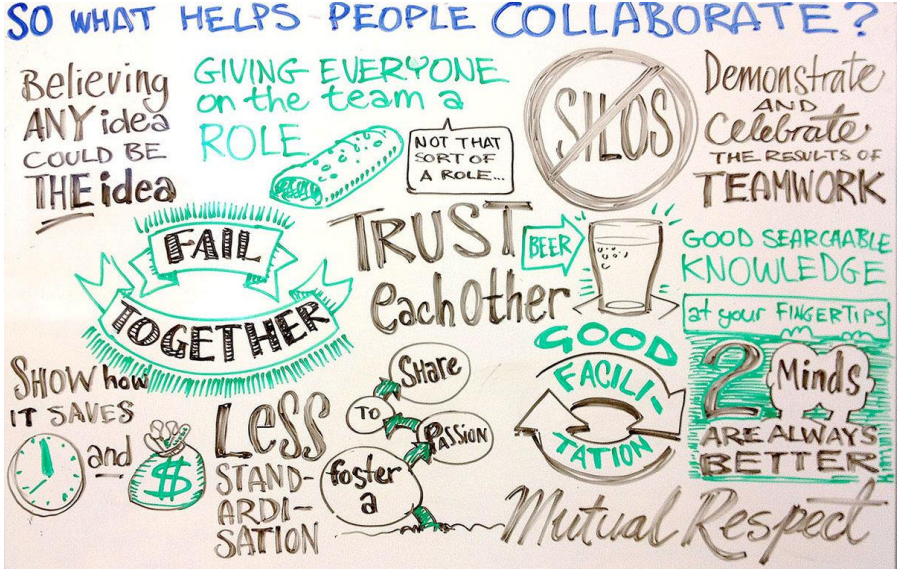
Italian research: room for improvement

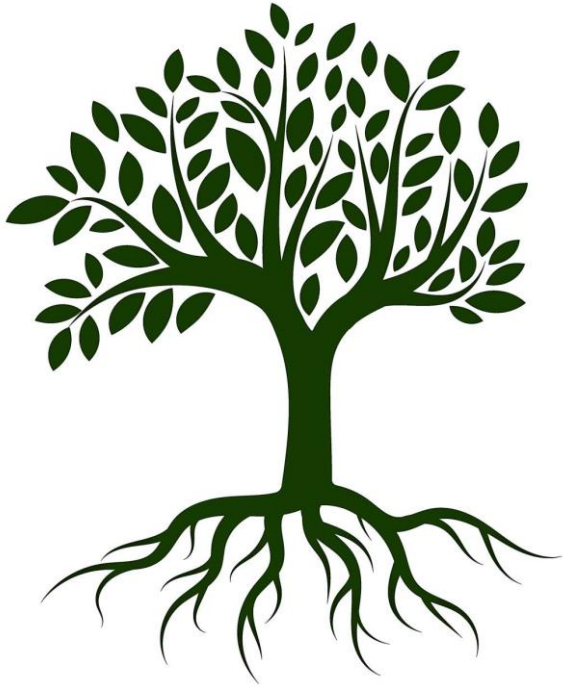
Join efforts for common goals



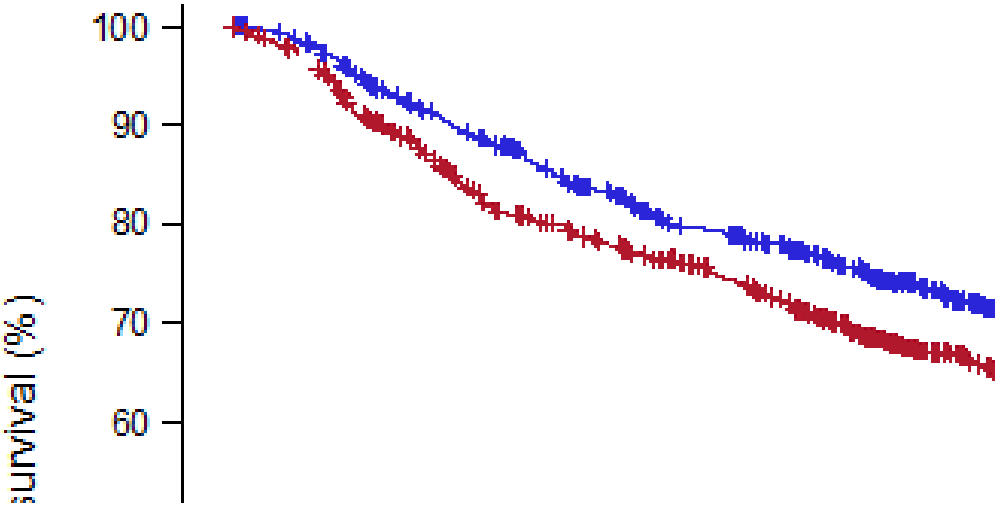
Italian research: room for improvement

- Improve the education of new generations of oncologist
- Engaging all the existing competences and expertises
- Improve quality of the research

Italian research: room for improvement



Example: improve quality by improving the commitment

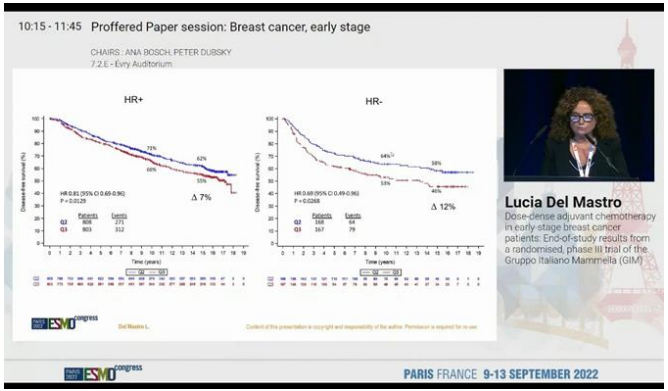


(Some) Next research questions in eBC

- Who benefit the most from dose-dense therapy?
- Which is the contribution of dose-dense AC in the context of dose-dense paclitaxel/carboplatin and olaparib administration (high-risk TNBC) ?
- Should dose-dense AC be used in combination with neoadjuvant immunotherapy in eTNBC?
- Any role for anthracyclines (and dose-dense AC) in HER2+ eBC?
- Who may be spared by anthracyclines in HER2-negative eBC?

Congratulations to Lucia, all co-authors GIM!

ESMO 2022



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When your ambition is big
Then your efforts should be even bigger

-unknown