QUESITO CLINICO 2:
In pazienti con carcinoma mammario HER2-positivo cT1 cN0 è raccomandabile trattamento neoadiuvante con chemioterapia e agente anti-HER2?

Sintesi delle evidenze e problematiche emerse (dal lavoro di gruppo)

Jennifer Foglietta

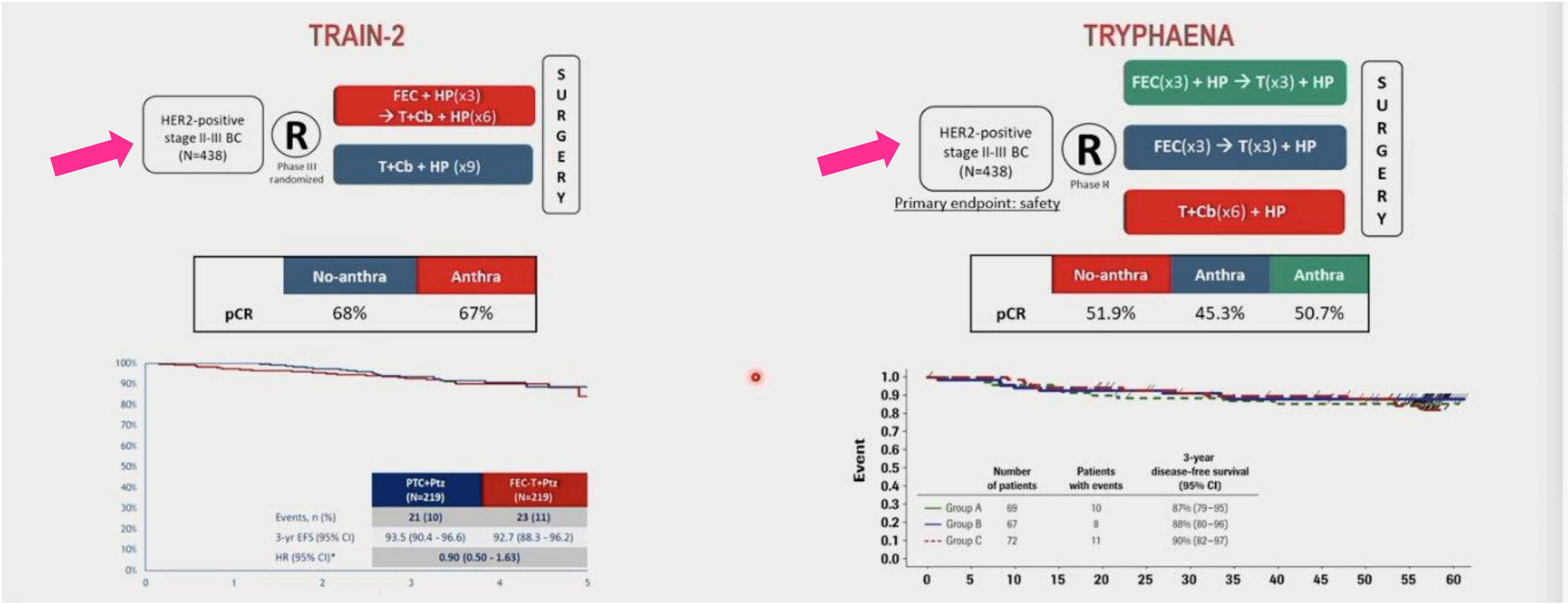
Ospedale S. Maria- Terni

- **P**= pazienti con carcinoma mammario HER-2 positivo cT1 cN0
- **I**= chemioterapia neoadiuvante+anti her2
- **C**= nessun trattamento neoadiuvante (chir.+adiuvante+ anti HER2)
- **O**=IDFS, DDFS, OS, qualità di vita e tossicità

Criteri inclusione

- NOHA trial:T>2cm
- NeoSphere: T >2 cm
- HannaH: breast clinical stage I to IIIC, including inflammatory and multicentric/multifocal breast cancer, with tumor size ≥1 cm
- TRYPHAENA: stage II-III
- BERENICE: T>2 cm se N0
- KRISTINE: T>2 cm
- PEONY: T2-3, N0-1, M0 or locally advanced breast cancer (T2-3, N2 or N3, M0; T4, any N, M0) and primary tumor larger than 2 cm

Antrhacycline-free regimens: neoadjuvant setting

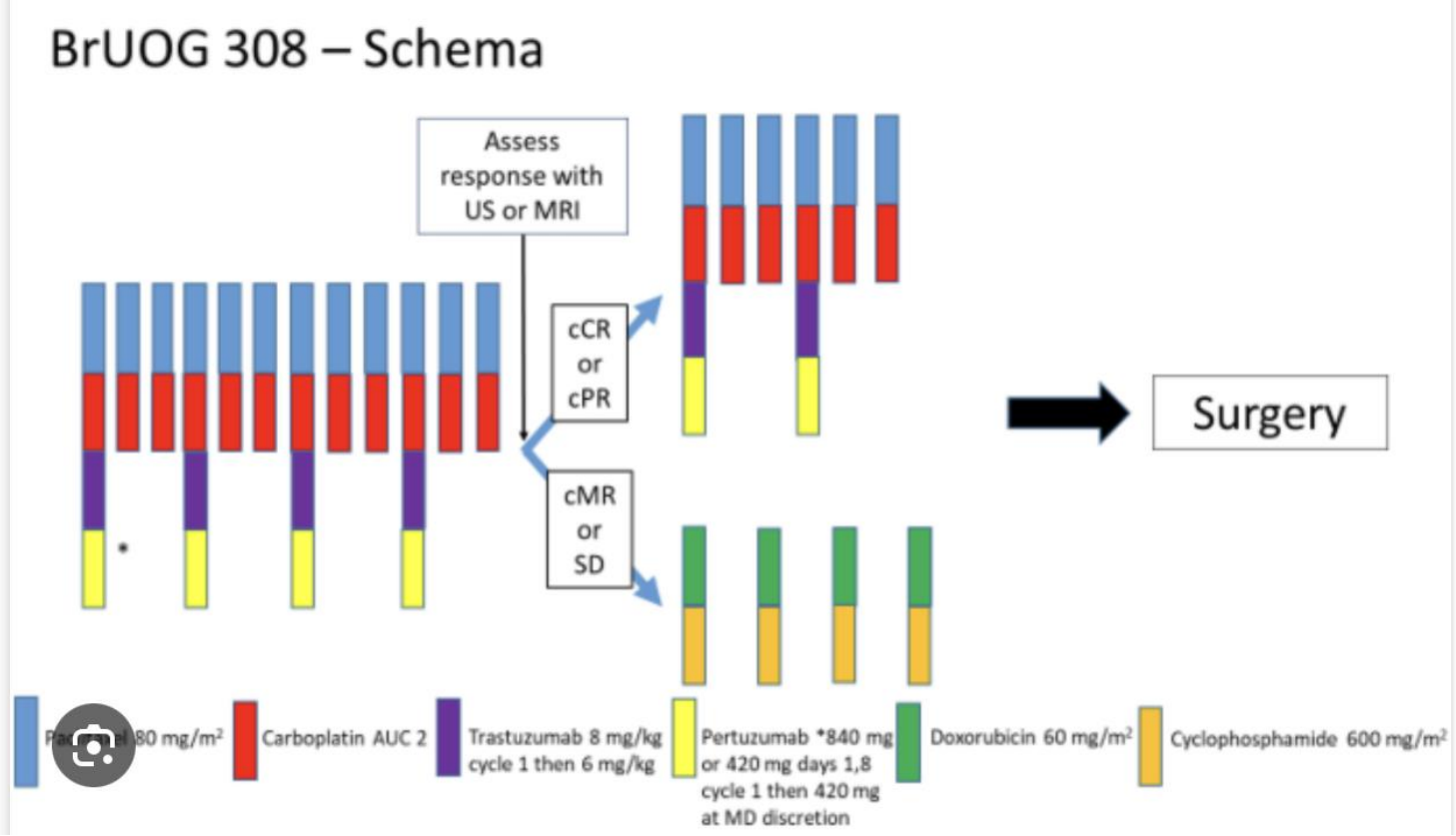


Van Ramshorst MS Lancet Oncol 2018

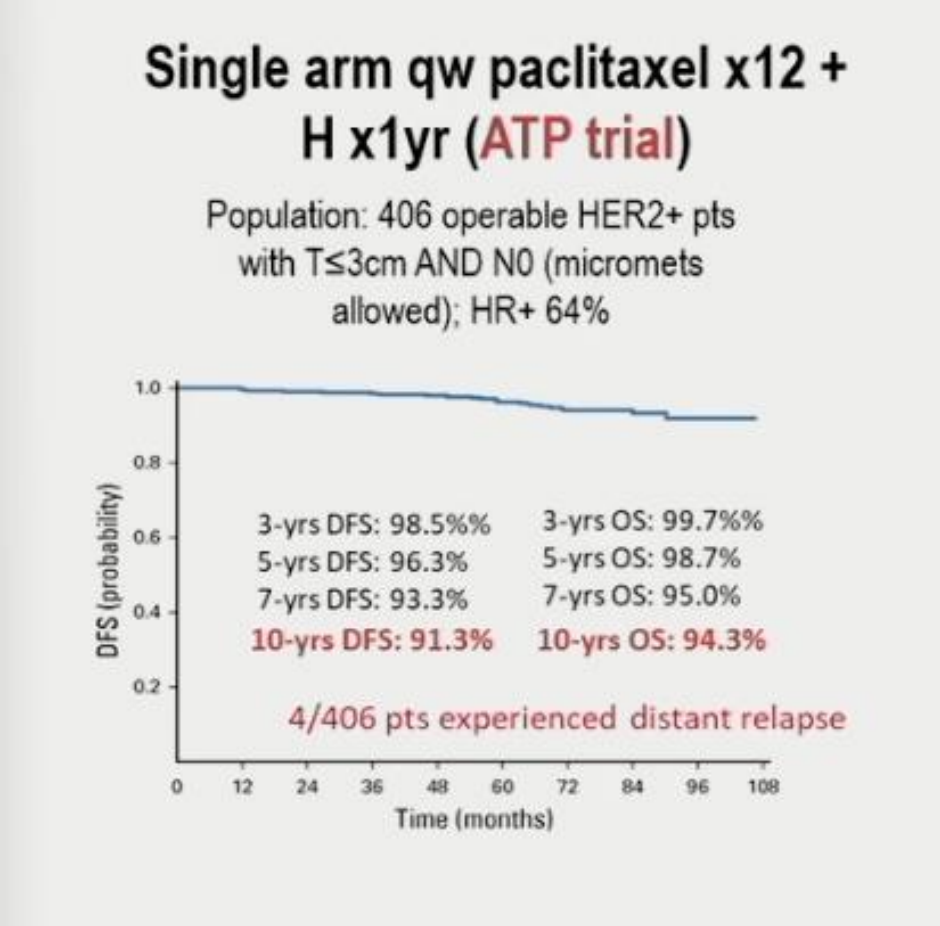
Schneeweiss et al Annal Oncol 2013

BrUOG study

clinical stage II-III HER2+ BC



Apt trial



10-year recurrence-free interval was 96·3% (95% CI 94·3–98·3)

10-year overall survival was 94·3% (95% CI 91·8–96·8)

10-year breast cancer-specific survival was 98·8% (95% CI 97·6–100).

Tolaney S. at al NEJM 2015; Lancet 2023

Processo di adolopment GRADE

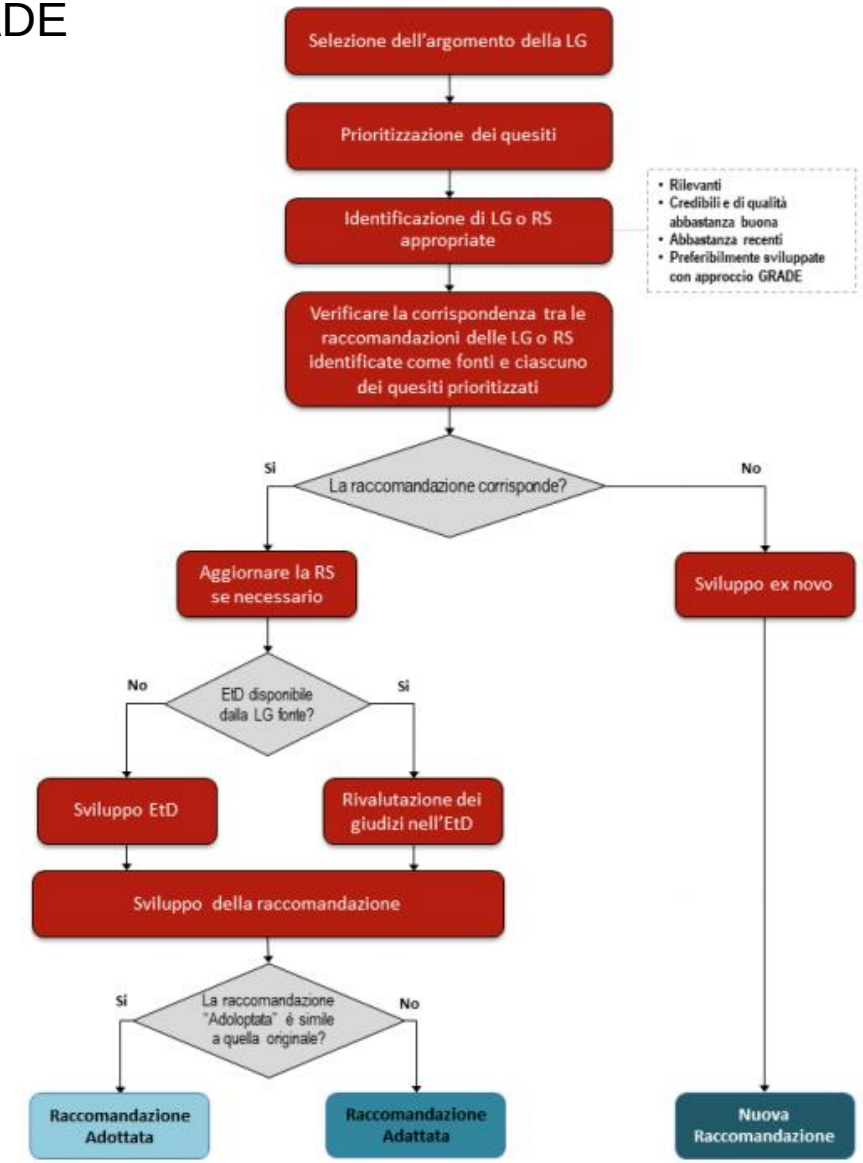


Figura 3 – Tradotta da: *Journal of Clinical Epidemiology* 2017 81, 101-110DOI: (10.1016/j.jclinepi.2016.09.009)

Neoadjuvant Chemotherapy, Endocrine Therapy, and Targeted Therapy for Breast Cancer: ASCO Guideline

Larissa A. Korde, MD[1]; Mark R. Somerfield, PhD[2]; Lisa A. Carey, MD[3]; Jennie R. Crews, MD[4]; Neelima Denduluri, MD[5]; E. Shelley Hwang, MD[6]; Seema A. Khan, MD[7]; Sibylle Loibl, MD, PhD[8]; Elizabeth A. Morris, MD[9]; Alejandra Perez, MD[10]; Meredith M. Regan, ScD[11]; Patricia A. Spears, BS[3]; Preeti K. Sudheendra, MD[12]; W. Fraser Symmans, MD[13]; Rachel L. Yung, MD[4]; Brittany E. Harvey, BS[2]; and Dawn L. Hershman, MD[14]

Recommendation 5.1. Patients with node-positive or high-risk node-negative, HER2-positive disease should be offered neoadjuvant therapy with an anthracycline and taxane or non–anthracycline-based regimen in combination with trastuzumab. Pertuzumab may be used with trastuzumab in the neoadjuvant setting (Type: evidence-based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).

Recommendation 5.2. Patients with T1a N0 and T1b N0, HER2-positive disease should not be routinely offered neoadjuvant chemotherapy or anti-HER2 agents outside of a clinical trial (Type: informal consensus; Evidence quality: intermediate; Strength of recommendation: moderate).

ORIGINAL ARTICLE

Nodal positivity and systemic therapy among patients with clinical T1–T2N0 human epidermal growth factor receptor-positive breast cancer: Results from two international cohorts

Anna Weiss MD[1,2,3,4] | Olga Martínez-Sáez MD, PhD[5,6] | Adrienne G. Waks MD[2,3,7] | Alison Laws MD, MPH[1,2,3] | Monica McGrath BA[1] | Paolo Tarantino MD[2,7] | Leah Portnow MD[2,3,8] | Eric Winer MD[2,3,7,9] | María Rey MD[5,6] | Marta Tapia MD[10] | Aleix Prat MD, PhD[5,6] | Ann H. Partridge MD, MPH[2,3,7] | Sara M. Tolaney MD, MPH[2,3,7] | Juan M. Cejalvo MD, PhD[10,11] | Elizabeth A. Mittendorf MD, PhD, MHCM[1,2,3] | Tari A. King MD[1,2,3]

- Registro Dana Farber (dal 2015-2020) n=579

- Registro spagnolo (Barcellona+Valencia) (2012-2021) n=292

Dati solo
Dana Farber

Should neoadjuvant chemotherapy and anti-HER2 vs. no neoadjuvant treatment be used for HER2 positive cT1 cNo breast cancer patients?

Bottom panel Explanations

Outcomes	Plain language statements	Absolute Effect: With no neoadjuvant treatment	Absolute Effect: With neoadjuvant chemotherapy and anti-HER2	Relative effect (95% CI)	Certainty of the evidence GRADE
Death	*Click here to add summary*	With no neoadjuvant treatment **1 out of 100** patients will develop an outcome and **99** would not.	With neoadjuvant chemotherapy and anti-HER2 **1 out of 100** patients will develop an outcome and **99** would not.	**RR** 1.16 (0.2 to 6.9)	⨁◯◯◯ VERY LOW. Due to serious risk of bias. Due to serious indirectness. Due to serious imprecision.
Recurrence					

Close

Difference: The difference between how many patients will develop an outcome with neoadjuvant chemotherapy and anti-HER2 and with no neoadjuvant treatment is **0 fewer patients out of 100**

Confidence interval: Due to the play of chance, there is uncertainty about this difference. The 95% confidence interval is **from 1 fewer to 5 more patients**

Dati solo
Dana Farber

Should neoadjuvant chemotherapy and anti-HER2 vs. no neoadjuvant treatment be used for HER2 positive cT1 cNo breast cancer patients?

Bottom panel Explanations

Outcomes	Plain language statements	Absolute Effect: With no neoadjuvant treatment	Absolute Effect: With neoadjuvant chemotherapy and anti-HER2	Relative effect (95% CI)	Certainty of the evidence GRADE
Death					
Recurrence	*Click here to add summary*	With no neoadjuvant treatment **1 out of 100** patients will develop an outcome and **99** would not.	With neoadjuvant chemotherapy and anti-HER2 **1 out of 100** patients will develop an outcome and **99** would not.	**RR 1.05** (0.25 to 4.34)	⨁◯◯◯ VERY LOW Due to serious risk of bias. Due to serious indirectness. Due to serious imprecision.

Close

Difference: The difference between how many patients will develop an outcome with neoadjuvant chemotherapy and anti-HER2 and with no neoadjuvant treatment is **0 fewer patients out of 100**

Confidence interval: Due to the play of chance, there is uncertainty about this difference. The 95% confidence interval is **from 1 fewer to 5 more patients**

Should neoadjuvant chemotherapy and anti-HER2 vs. no neoadjuvant treatment be used for HER2 positive cT1 cNo breast cancer patients?

Bottom panel | Explanations

Outcomes	Plain language statements	With no neoadjuvant treatment	With neoadjuvant chemotherapy and anti-HER2	Relative effect (95% CI)	Certainty of the evidence GRADE
Death					
Recurrence					
axillary lymph node dissection	*Click here to add summary*	With no neoadjuvant treatment **9 out of 100** patients will develop an outcome and **91** would not.	With neoadjuvant chemotherapy and anti-HER2 **9 out of 100** patients will develop an outcome and **91** would not.	**RR 1** (0.51 to 1.95)	⨁◯◯◯ VERY LOW Due to serious risk of bias. Due to serious inconsistency. Due to serious indirectness. Due to serious imprecision.

Close

Difference: The difference between how many patients will develop an outcome with neoadjuvant chemotherapy and anti-HER2 and with no neoadjuvant treatment is **0 fewer patients out of 100**

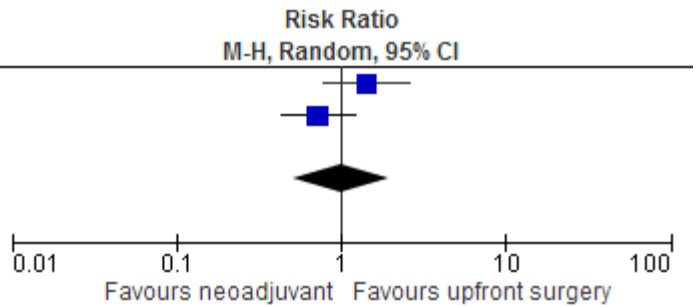
Confidence interval: Due to the play of chance, there is uncertainty about this difference. The 95% confidence interval is **from 5 fewer to 9 more patients**

Axillary lymph node dissection

Study or Subgroup	neoadjuvant Events	Total	upfront surgery Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
DF/BCC	18	211	22	368	47.6%	1.43 [0.78, 2.60]
HCB/HCV	24	173	23	119	52.4%	0.72 [0.43, 1.21]
Total (95% CI)		**384**		**487**	**100.0%**	**1.00 [0.51, 1.95]**
Total events	42		45			

Heterogeneity: $Tau^2 = 0.15$; $Chi^2 = 2.88$, df = 1 (P = 0.09); $I^2 = 65\%$

Test for overall effect: Z = 0.01 (P = 0.99)



Should neoadjuvant chemotherapy and anti-HER2 vs. no neoadjuvant treatment be used for HER2 positive cT1 cNo breast cancer patients?

Bottom panel | Explanations

Death

Recurrence

axillary lymph node dissection

nodal involvement

Click here to add summary

With no neoadjuvant treatment **18 out of 100** patients will develop an outcome and **82** would not.

With neoadjuvant chemotherapy and anti-HER2 **14 out of 100** patients will develop an outcome and **86** would not.

Close

Difference: The difference between how many patients will develop an outcome with neoadjuvant chemotherapy and anti-HER2 and with no neoadjuvant treatment is **4 fewer patients out of 100**

Confidence interval: Due to the play of chance, there is uncertainty about this difference. The 95% confidence interval is **from 10 fewer to 5 more patients**

RR 0.76
(0.45 to 1.29)

⊕OOO
VERY LOW

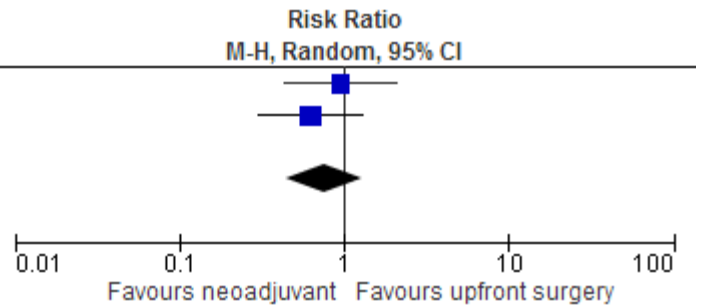
Due to serious risk of bias.
Due to serious imprecision.

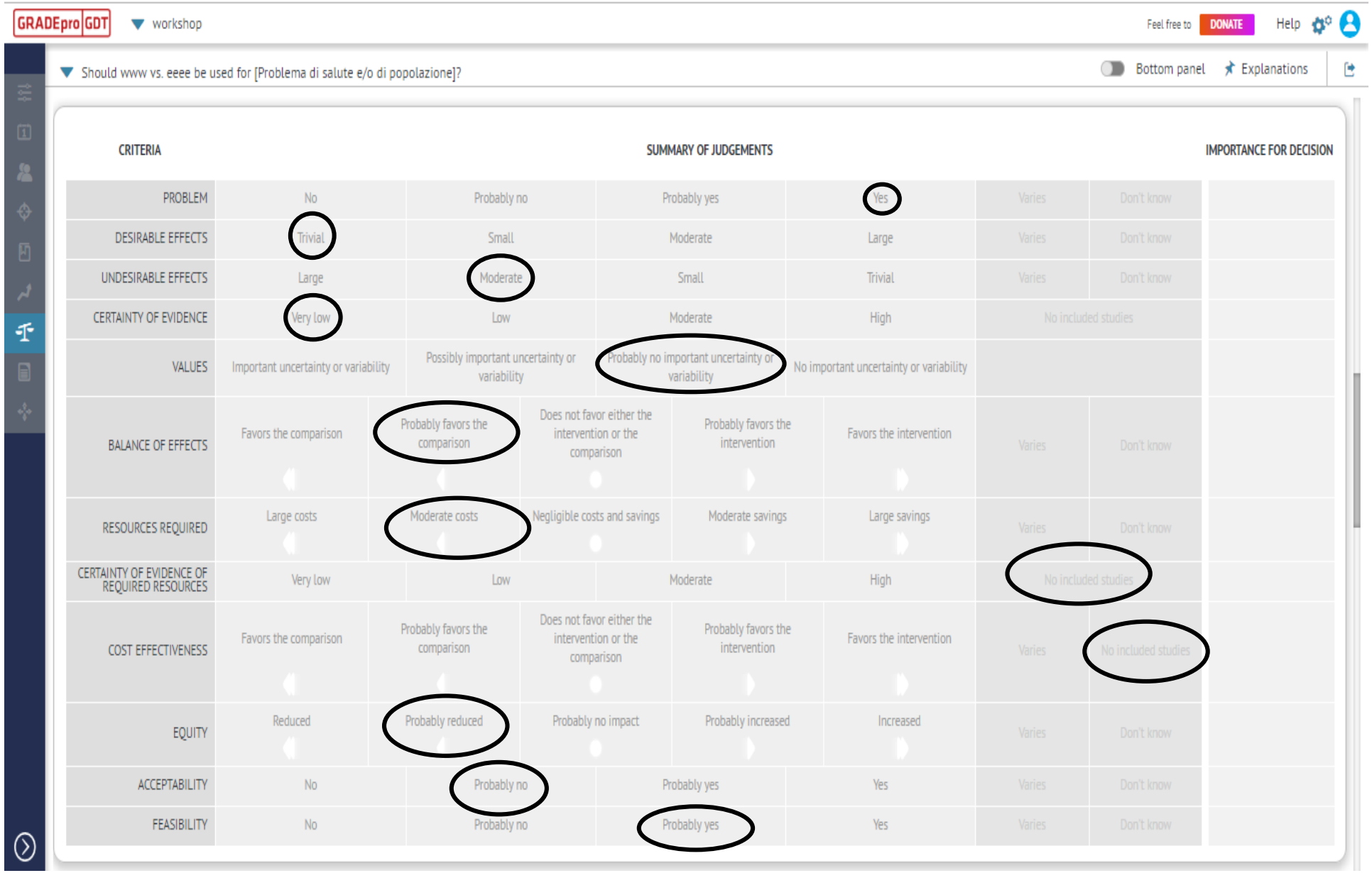
Nodal involvement

Study or Subgroup	neoadjuvant Events	Total	upfront surgery Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
DF/BCC	6	37	54	315	47.0%	0.95 [0.44, 2.05]
HCB/HCV	9	72	20	100	53.0%	0.63 [0.30, 1.29]
Total (95% CI)		**109**		**415**	**100.0%**	**0.76 [0.45, 1.29]**
Total events	15		74			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.59$, df = 1 (P = 0.44); $I^2 = 0\%$

Test for overall effect: Z = 1.02 (P = 0.31)




GRADEpro GDT
workshop
Feel free to
DONATE
Help
Should www vs. eeee be used for [Problema di salute e/o di popolazione]?
Bottom panel
Explanations
CRITERIA
SUMMARY OF JUDGEMENTS
IMPORTANCE FOR DECISION
PROBLEM
No
Probably no
Probably yes
Yes
Varies
Don't know
DESIRABLE EFFECTS
Trivial
Small
Moderate
Large
Varies
Don't know
UNDESIRABLE EFFECTS
Large
Moderate
Small
Trivial
Varies
Don't know
CERTAINTY OF EVIDENCE
Very low
Low
Moderate
High
No included studies
VALUES
Important uncertainty or variability
Possibly important uncertainty or variability
Probably no important uncertainty or variability
No important uncertainty or variability
BALANCE OF EFFECTS
Favors the comparison
Probably favors the comparison
Does not favor either the intervention or the comparison
Probably favors the intervention
Favors the intervention
Varies
Don't know
RESOURCES REQUIRED
Large costs
Moderate costs
Negligible costs and savings
Moderate savings
Large savings
Varies
Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES
Very low
Low
Moderate
High
No included studies
COST EFFECTIVENESS
Favors the comparison
Probably favors the comparison
Does not favor either the intervention or the comparison
Probably favors the intervention
Favors the intervention
Varies
No included studies
EQUITY
Reduced
Probably reduced
Probably no impact
Probably increased
Increased
Varies
Don't know
ACCEPTABILITY
No
Probably no
Probably yes
Yes
Varies
Don't know
FEASIBILITY
No
Probably no
Probably yes
Yes
Varies
Don't know

Raccomandazione: condizionata a sfavore con certezza delle prove molto bassa

NAT in cT1 cN0 non dovrebbe essere presa in considerazione come prima opzione