DISCUSSIONE SULLA QUALITÁ E SULLA RILEVANZA CLINICA DELLE EVIDENZE

QUESITO GRADE 1: Nelle pazienti con carcinoma mammario N+ operato, la chemioterapia dose-dense è raccomandabile rispetto alla chemioterapia standard?

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Come valutare la Qualità delle Evidenze disponibili in Letteratura

Determinants of quality

5 factors that can lower quality

1. limitations of detailed design and execution *(risk of bias criteria)*
2. Inconsistency *(or heterogeneity)*
3. Indirectness *(PICO and applicability)*
4. Imprecision *(number of events and confidence intervals)*
5. Publication bias

The members of the Grade Working Group

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Graduazione della qualità delle prove.

Livello qualità	Significato	Conseguenza
Alta	Alto grado di confidenza nei risultati	È molto improbabile che ulteriori studi possano cambiare la fiducia nella stima di effetto
Moderata	Discreto grado di confidenza nei risultati	È probabile che ulteriori studi possano confermare o cambiare la fiducia nella stima di effetto
Bassa	I risultati sono poco credibili	È necessaria ulteriore ricerca per ottenere stime affidabili sugli effetti positivi e negativi dell'intervento
Molto bassa	I dati esaminati sono totalmente inaffidabili	Non è possibile fare affidamento sulle stime di effetto disponibili

RCTs ⊕⊕⊕⊕ observational studies ⊕⊕◯◯

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Come valutare la Qualità delle Evidenze disponibili in Letteratura

Author(s): MC IC
Date: 2015-03-25
Question: Should dose-dense antraciclines/taxanes based chemotherapy vs conventional chemotherapy be used in N-positive breast cancer patients?
Settings:
Bibliography: Citron M, JCO 2003; 21:1431-1439 Burnell M, JCO 2010; 28:77-82 Moebus V, JCO 2010; 28:2874-2880 Swain SM, JCO 2013; 31:3197-3204 Del Mastro L, TheLancet 2015; published online 2nd march

OUTCOME di BENEFIOCIO: OS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dose-dense antraciclines/taxanes based chemotherapy	Conventional chemotherapy	Relative (95% CI)	Absolute		
OS - Citron 2003 (follow-up median 36 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	75/988 (7.6%)	107/985 (10.9%)	HR 0.81 (0.66 to 1)	2 fewer per 100 (from 4 fewer to 0 more)	⊕⊕⊕O MODERATE	CRITICAL
OS - Burnell 2010 - not re												
												CRITICAL
OS - Moebus 2010 (follow-up median 62 months)												
1	randomised trials	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	114/641 (17.8%)	139/611 (22.7%)	HR 0.76 (0.59 to 0.97)	5 fewer per 100 (from 1 fewer to 9 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
OS - Swain 2013 (follow-up median 64 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	167/1618 (10.3%)	185/1617 (11.4%)	HR 0.86 (0.7 to 1.07)	2 fewer per 100 (from 3 fewer to 1 more)	⊕⊕⊕O MODERATE	CRITICAL
OS - Del Mastro 2015 (follow-up median 7 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	103/1002 (10.3%)	149/1001 (14.9%)	HR 0.65 (0.51 to 0.84)	5 fewer per 100 (from 2 fewer to 7 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL

[1] It was not possible to judge the the whole risk of bias of the study because of lack of information. We considered an UNCLEAR risk for all bias

OUTCOME DI BENEFICIO: DFS

DFS - Citron 2003 (follow-up median 36 months)												
1	randomised trials	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	136/988 (13.8%)	179/985 (18.2%)	HR 0.50 (0.3 to 0.83)	9 fewer per 100 (from 3 fewer to 12 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
DFS - Burnell 2010 (follow-up median 30.4 months)												
1	randomised trials	no serious risk of bias[1]	no serious inconsistency	serious[3]				105/702 (15%)	HR 0.59 (0.44 to 0.8)	6 fewer per 100 (from 3 fewer to 8 fewer)	⊕⊕⊕O MODERATE	CRITICAL
DFS - Moebus 2010 (follow-up median 62 months)												
1	randomised trials	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	182/641 (28.4%)	226/611 (37%)	HR 0.72 (0.59 to 0.87)	9 fewer per 100 (from 4 fewer to 13 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
DFS - Swain 2013 (follow-up median 62 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	320/1613 (19.8%)	327/1610 (20.3%)	HR 0.93 (0.8 to 1.09)	1 fewer per 100 (from 4 fewer to 2 more)	⊕⊕⊕⊕ HIGH	CRITICAL
DFS - Del Mastro 2015 (follow-up median 7 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	224/1002 (22.4%)	270/1001 (27%)	HR 0.77 (0.65 to 0.92)	5 fewer per 100 (from 2 fewer to 8 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL

[3] 28% of patients in both arms were node negative

OUTCOME DI DANNO: ANEMIA

[1] It was not possible to judge the the whole risk of bias of the study because of lack of information. We considered an UNCLEAR risk for all bias

[4] We decided to not downgrade quality of evidence for imprecision due to the low number of events in both arms

Anemia (grade 3/4) - Cit						**with: Hemogl**						
1	randomised trials	no serio bias[1]			no serious imprecision[4]					wer per 100 (from 0 fewer to 1 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Anemia (grade 3/4) - Burnell 2010 (follow-up median 30.4 months; assessed with: Hemoglobin)												
1	randomised trials	no serious risk of bias[1]	no serious inconsistency	serious[3]	no serious imprecision	none	199/687 (29%)	7/674 (1%)	RR 27.89 (58.82 to 13.22)	28 more per 100 (from 13 more to 60 more)	⊕⊕⊕O MODERATE	IMPORTANT
Anemia (grade 3/4) - Moebus 2010 (follow-up median 62 months)												
1	randomised trials	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	53/623 (8.5%)	6/587 (1%)	RR 8.32 (3.61 to 19.22)	7 more per 100 (from 3 more to 19 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Anemia (grade 3/4) - Swain 2013 (follow-up median 64 months; assessed with: not reported)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[4]	none	25/1612 (1.6%)	3/1607 (0.19%)	RR 2.31 (2.51 to 27.46)	0 more per 100 (from 0 more to 5 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Anemia (grade 3/4) - Del Mastro 2015 (follow-up median 7 years; assessed with: not reported)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	14/988 (1.4%)	2/984 (0.2%)	RR 6.97 (1.59 to 30.6)	1 more per 100 (from 0 more to 6 more)	⊕⊕⊕⊕ HIGH	IMPORTANT

OUTCOME DI DANNO: NEUTROPENIA FEBBRILE

Febrile neutropenia (grade 3/4) - Citron 2003 - not reported												
Febrile neutropenia (grade 3/4) - Burnell 2010 (follow-up median 30.4 months)												
1	randomised trials	no serious risk of bias[1]	no serious inconsistency	serious[3]	no serious imprecision	none	111/701 (15.8%)	32/702 (4.6%)	RR 3.47 (2.37 to 5.07)	11 more per 100 (from 6 more to 19 more)	⊕⊕⊕O MODERATE	IMPORTANT
Febrile neutropenia (grade 3/4) - Moebus 2010 (follow-up median 62 months)												
1	randomised trials	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	44/623 (7.1%)	12/587 (2%)	RR 3.45 (1.84 to 6.48)	5 more per 100 (from 2 more to 11 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Febrile neutropenia (grade 3/4) - Swain 2013 (follow-up median 64 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	51/1612 (3.2%)	144/1607 (9%)	RR 0.35 (0.26 to 0.48)	6 fewer per 100 (from 5 fewer to 7 fewer)	⊕⊕⊕⊕ HIGH	IMPORTANT
Febrile neutropenia (grade 3/4) - Del Mastro 2015 - not reported												
												IMPORTANT

OUTCOME DI DANNO: RISCHIO LEUCEMICO

Acute leucosis/myelodysplasia (grade 3/4) - Citron 2003 - not reported												
1	-	-	-	-	-				-	-		
Acute leucosis/myelodysplasia (grade 3/4) - Burnell 2010 (follow-up median 30.4 months)												
1	randomised trials	no serious risk of bias[1]	no serious inconsistency	serious[3]	no serious imprecision[4]	none	4/701 (0.57%)	0/702 (0%)	RR 8.01 (0.42 to 151.26)	-	⊕⊕⊕O MODERATE	IMPORTANT
Acute leucosis/myelodysplasia (grade 3/4) - Moebus 2010 (follow-up median 62 months)												
1	randomised trials	no serious risk of bias[1]	no serious inconsistency	no serious indirectness	no serious imprecision[4]	none	4/623 (0.64%)	0/587 (0%)	RR 7.54 (0.40 to 142.27)	-	⊕⊕⊕⊕ HIGH	IMPORTANT
Acute leucosis/myelodysplasia (grade 3/4) - Swain 2013 (follow-up median 64 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[4]	none	11/1612 (0.68%)	5/1607 (0.31%)	RR 2.19 (0.76 to 6.30)	0 more per 100 (from 0 fewer to 2 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Acute leucosis/myelodysplasia (grade 3/4) - Del Mastro 2015 (follow-up median 7 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[4]	none	2/988 (0.2%)	0/984 (0%)	RR 3.98 (0.18 to 88.24)	-	⊕⊕⊕⊕ HIGH	IMPORTANT

GRAZIE PER L'ATTENZIONE

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