Terapia neoadiuvante

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Meta analysis

Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 93 randomised trials and 17,346 patients

Jean-Pierre Pignon [a,*], Aurélie le Maître [a], Emilie Maillard [a], Jean Bourhis [b], on behalf of the MACH-NC Collaborative Group [1]

Chemioterapia: 4,5% a 5 anni

Chemioterapia concomitante: 6.5% a 5 anni

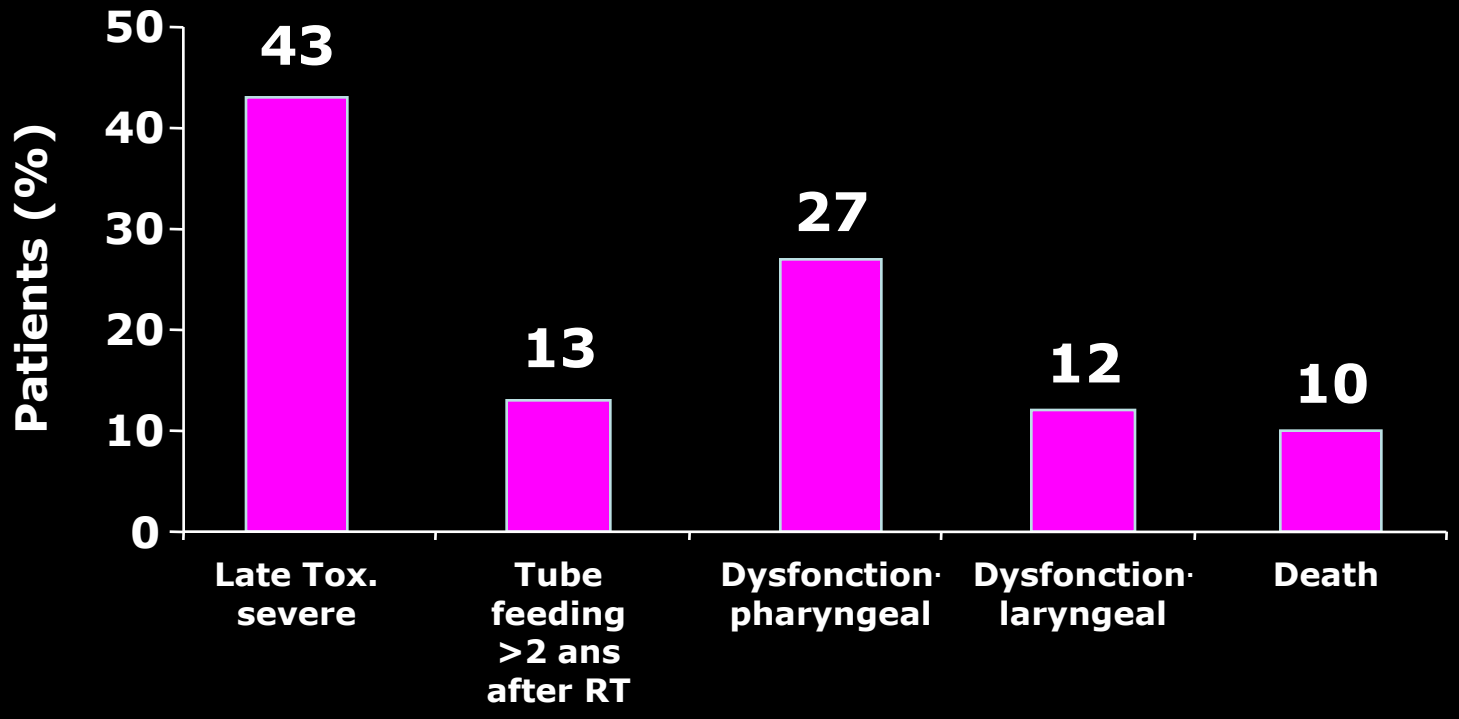
Chemioterapia di induzione: 2,4% a 5 anni

CRT concomitante

- **Aumenta controllo locale e sopravvivenza in HNC e NPC (trials e meta-analisi)**
- **MACH-NC*: beneficio in tutte le situazioni cliniche (inclusa RT post-op, CRT frazionamento alterato)**
- **Schedula di riferimento: cisplatino 100 mg/mq giorni 1, 22 e 43**
- **Schedula impiegata per preservazione d'organo**
- **Post-op**: linfonodi ECS +, R1 o margine close**

Pignon, 2009;
***** Bernier, 2005***

RT-CT arm of 3 RTOG trials (91-11, 97-03 et 99-14)



Machtay, JCO 2008

Taxotere + PF

Autore, aa	Schema	N° pz	Ph	RR%	Tox ≥ G3%	DM%	Median PFS mo	Median OS mo
Vermorken, NEJM 2007 TAX 323	TPF vs-> RT PF	358	III	72* 59	77 N 42 GB	13 10	11* 8	19* 14
Posner, NEJM 2007 TAX 324	TPF vs->CRT§ PF	501	III	72** 64	83 N	5 9	36* 13	71* 30
Paccagnella, Ann Onc 2010	TPF->CRT vs CRT	101	II	78* 83	52 N	nr nr	30 20	40 33

*** dopo chemioterapia di induzione*

TPF per preservazione d'organo

Autore, aa	Schema	N° pz	Ph	3-yr LP%	Tox ≥ G3%	DM	3-yr DFS%	3-yr OS%
Pointreau, JNCI 2009	TPF vs-> RT* PF	213	III	70* 57	31 N	12 16	58 44	60 60

Autore, aa	Schema	N° pz	Ph	3-yr LFS%	Tox ≥ G3%	DM	3-yr PFS%	3-yr OS%
Posner, Ann Oncol 2009	TPF vs-> RT PF	166		52 32	nr	5 5	38 32	49 35

National Comprehensive Cancer Network®

JNCCN

JNCCN.org Journal of the National Comprehensive Cancer Network

Head and Neck Cancers

David G. Pfister, Kie-Kian Ang, David M. Brizel, Barbara A. Burtness, Anthony J. Cmelak, A. Dimitrios Colevas, Frank Dunphy, David W. Eisele, Jill Gilbert, Maura L. Gillison, Robert I. Haddad, Bruce H. Haughey, Wesley L. Hicks, Jr., Ying J. Hitchcock, Merrill S. Kies, William M. Lydiatt, Ellie Maghami, Renato Martins, Thomas McCaffrey, Bharat B. Mittal, Harlan A. Pinto, John A. Ridge, Sandeep Samant, Giuseppe Sanguineti, David E. Schuller, Jatin P. Shah, Sharon Spencer, Andy Trotti III, Randal S. Weber, Gregory T. Wolf and Frank Worden

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NCCN Categories of Evidence and Consensus

Category 1: The recommendation is based on high-level evidence (e.g., randomized controlled trials) and there is uniform NCCN consensus.

Category 2A: The recommendation is based on lower-level evidence and there is uniform NCCN consensus.

Category 2B: The recommendation is based on lower-level evidence and there is nonuniform NCCN consensus (but no major disagreement).

Category 3: The recommendation is based on any level of evidence but reflects major disagreement.

Hypopharynx

- T2 N0 selected (TL required)
- T1 N+
- T2-3 any N
- T4a any N (category 3)

Supraglottic larynx

- T3 N0 (TL required) category 3
- T1-2 N+
- T3 N1 selected } (TL not required) category 3
- T3 N2-N3 (TL required) category 2B
- T4a N0-N3 (pts who decline TL) category 2B

Glottic Larynx

- T3 (TL) N2-3 category 3
- T4a any T (pts who decline TL) category 2B

Oropharynx

- T3-T4a N0-1 category 3
- Any T N2-3 category 2B

ESMO guidelines

The role of induction chemotherapy (ICT) has been reconsidered since the introduction of taxane–platinum-based (TPF) combinations that have proved to be superior to platinum–fluorouracil PF schedule in loco-regionally advanced disease [I, A]. However, at present, induction chemotherapy is not considered standard treatment in advanced disease. ICT followed by RT-CT (so-called sequential CT-RT) is still under evaluation. The overall toxicity of this approach can be substantial thus compromising the final result.

TPF induction chemotherapy followed by radiotherapy in responsive patients is an option for organ preservation in advanced larynx and hypopharynx cancer in patients otherwise requiring total laryngectomy [II, A]. CRT is another option. In

Gregoire V, Ann Oncol 2010

Il profilo molecolare.....

The NEW ENGLAND JOURNAL of MEDICINE

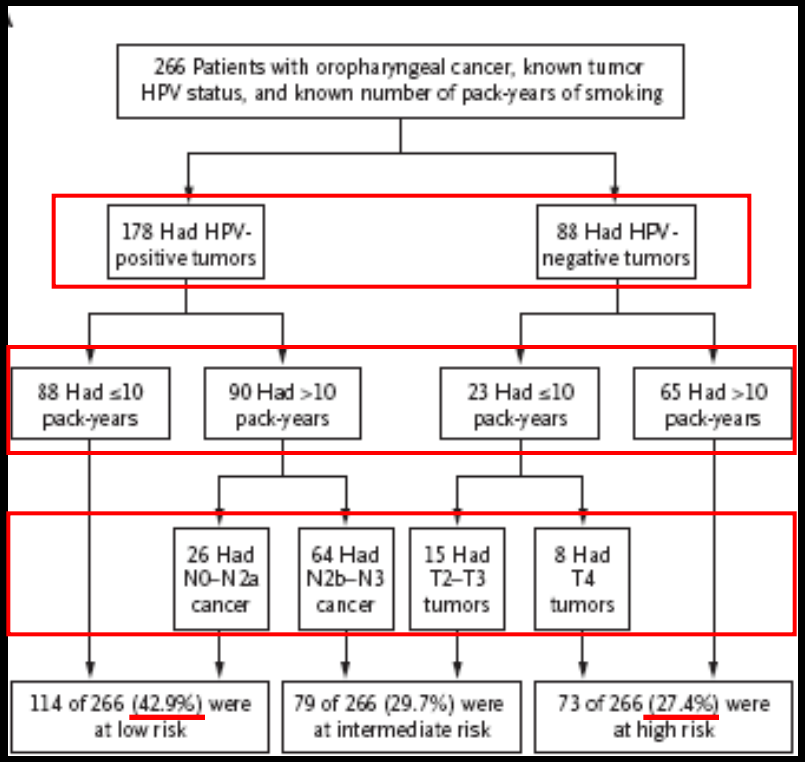
ORIGINAL ARTICLE

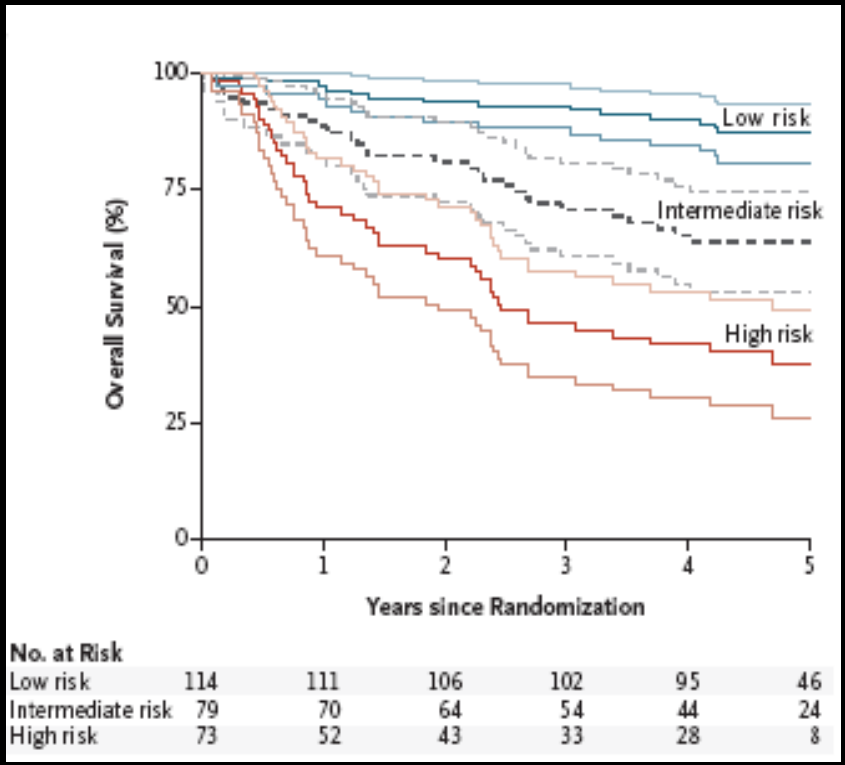
Human Papillomavirus and Survival of Patients with Oropharyngeal Cancer

K. Kian Ang, M.D., Ph.D., Jonathan Harris, M.S., Richard Wheeler, M.D., Randal Weber, M.D., David I. Rosenthal, M.D., Phuc Felix Nguyen-Tân, M.D., William H. Westra, M.D., Christine H. Chung, M.D., Richard C. Jordan, D.D.S., Ph.D., Charles Lu, M.D., Harold Kim, M.D., Rita Axelrod, M.D., C. Craig Silverman, M.D., Kevin P. Redmond, M.D., and Maura L. Gillison, M.D., Ph.D.

RISK	HPV+	HPV-
Low	≤ 10 smoked packs /year > 10 smoked packs /year if < N2b	
Interm	> 10 smoked packs /year if ≥ N2b	≤ 10 smoked packs /year and < T4
High		> 10 smoked packs/year or T4

10 packs/year=20 sig/die per 10 anni


266 Patients with oropharyngeal cancer, known tumor HPV status, and known number of pack-years of smoking
178 Had HPV-positive tumors
88 Had HPV-negative tumors
88 Had ≤10 pack-years
90 Had >10 pack-years
23 Had ≤10 pack-years
65 Had >10 pack-years
26 Had N0–N2a cancer
64 Had N2b–N3 cancer
15 Had T2–T3 tumors
8 Had T4 tumors
114 of 266 (42.9%) were at low risk
79 of 266 (29.7%) were at intermediate risk
73 of 266 (27.4%) were at high risk


Overall Survival (%)
100
75
50
25
0
Low risk
Intermediate risk
High risk
0
1
2
3
4
5
Years since Randomization
No. at Risk
Low risk 114 111 106 102 95 46
Intermediate risk 79 70 64 54 44 24
High risk 73 52 43 33 28 8

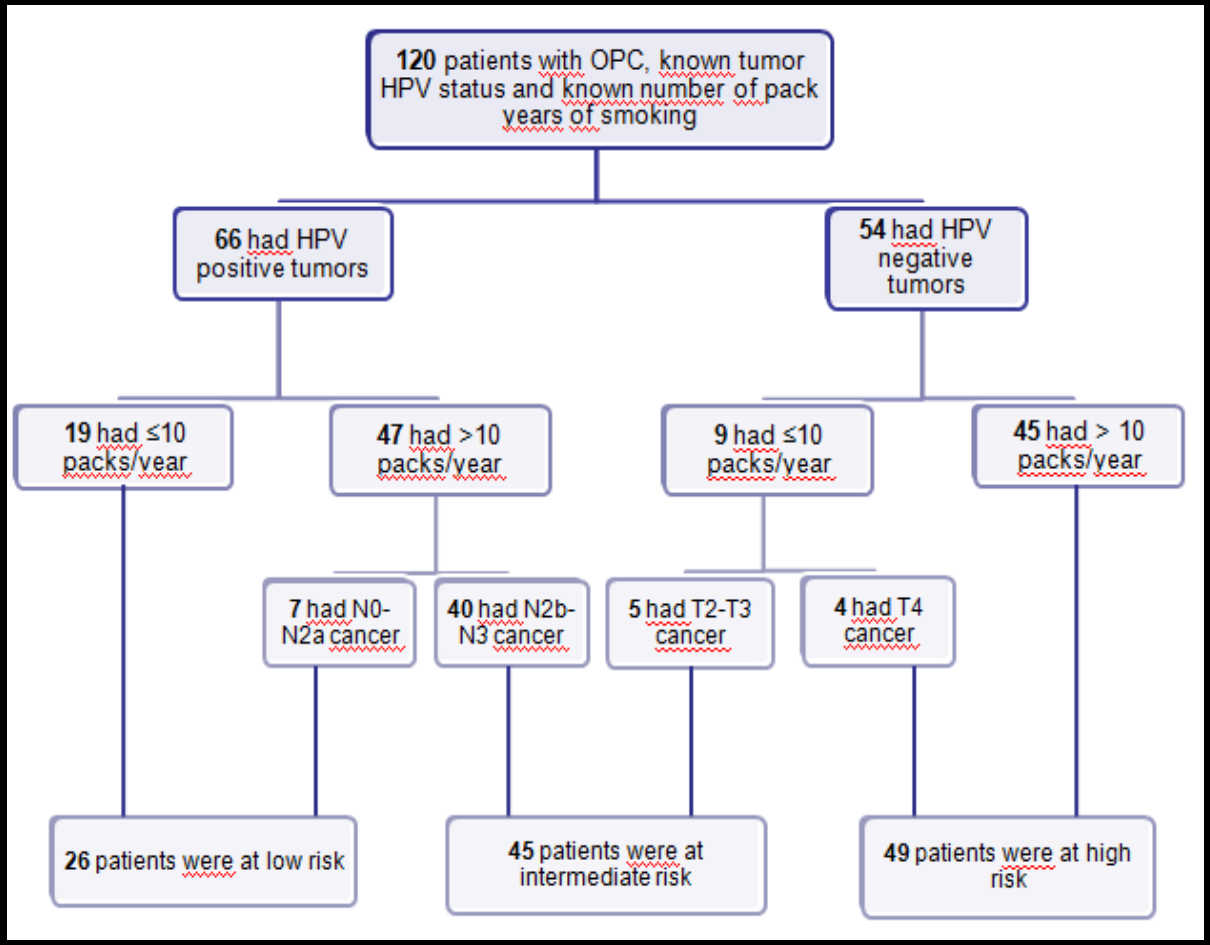
Annals of Oncology Advance Access published December 21, 2011

original article

Annals of Oncology
doi:10.1093/annonc/mdr544

Tumor stage, human papillomavirus and smoking status affect the survival of patients with oropharyngeal cancer: an Italian validation study

R. Granata[1], R. Micelli[2], E. Orlandi[3], F. Perrone[4], B. Cortelazzi[4], M. Franceschini[3], L. D. Locati[1], P. Bossi[1], C. Bergamini[1], A. Mirabile[1], L. Mariani[2], P. Olmi[3], G. Scaramellini[5], P. Potepan[6], P. Quattrone[7], K. K. Ang[8] & L. Licitra[1]*


120 patients with OPC, known tumor HPV status and known number of pack years of smoking
66 had HPV positive tumors
54 had HPV negative tumors
19 had ≤10 packs/year
47 had >10 packs/year
9 had ≤10 packs/year
45 had > 10 packs/year
7 had N0-N2a cancer
40 had N2b-N3 cancer
5 had T2-T3 cancer
4 had T4 cancer
26 patients were at low risk
45 patients were at intermediate risk
49 patients were at high risk

22%

41%

Preoperative TPF chemotherapy in locally advanced resectable oral cavity squamous cell cancer: a phase II study.

Standard treatment

- Surgery followed by radiotherapy or concomitant chemo-radiotherapy (high-risk cases) is the standard therapy

- In a phase III study PF primary chemotherapy followed by standard treatment didn't improve overall survival over standard therapy (Licitra L, JCO 2003; Bossi P, 2006)

Biological markers

- Pathological complete remission (pCR) correlates with a good prognosis.
- In oral cavity cancer pCR has been recorded in 40% of cases (all TP53 wild-type) (Perrone F, JCO 2010)
- Overexpression of beta-T II is related to a worse outcome in HNSCC and other type of malignant tumors and to taxane resistance
- Low expression of beta-T II seems to predict the benefit from TPF

AIMS

Primary endpoint

- Rate of pathological complete response to CT (TP53 wild type and/or low expression of beta-T II)

Secondary endpoints

- Compliance to induction chemo and toxicity
- Early functional response evaluation by DWI and DCE MRI
- Comparison between (DWI - DCE) MRI response and pathological response
- Percentage of patient receiving postoperative radiotherapy and chemotherapy
- Progression free survival and overall survival
- Second primary tumour incidence

SAMPLE SIZE: 64 patients

Conclusioni

- **Chemioterapia di induzione non è lo standard**
- **Criteri di selezione**
- **Biologia molecolare**