

Concurrent chemoradiation (CCRT) or radiotherapy (RT) with anti-EGFR directed monoclonal antibody (anti-EGFR) or CCRT + anti-EGFR in locoregionally advanced squamous cell carcinoma of the head and neck (LA-HNSCC): a comprehensive review of randomized data

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Introduction

Several randomized trials on the relative role of CCRT and RT with anti-EGFR were recently published/presented.

Aim

To summarize the existing literature on the role of anti-EGFR directed antibodies as compared to or in association with CCRT.

References

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Results

We retrieved 10 randomized trials from the literature and major congresses (table).

Study author	Phase	N	RT dose and n	Study arms	LRC	OS	PFS	SAE	Grade 3-4 toxicities			Interruption > 10 days	Dose reductions
									Dysphagia	Mucositis	Dermatitis		
CCRT or RT + anti-EGFR													
Concert-2	II	61	70-72 Gy, 30-32	cisplatin 100 mg/m ² x 2	61%*			40%	32%	40%	11%	0%	32% ^{oo}
Giralt		90		panitumumab 9 mg/kg x 3	51%*			34%	40%	42%	24%	7%	45% ^{oo}
Magrini	II	35	70 Gy, 35	cisplatin 40 mg/m ² /week	80%			3%*		53%	21%	0%*	53%*
		35		cetuximab	53%			19%*		59%	44%	13%*	34%*
									p = 0.044		p = 0.039		p = 0.05
Hitt	III	205	70 Gy, 35	TPF x 2/3=>cisplatin 100 mg/m ² x 3	55.6%	61.3%* ^{ooo}		28.8%	6.3%	31.7%	2.0%	85%	
		202		TPF x 2/3=>cetuximab	50.1%	54.1%* ^{ooo}		22.8%	4.5%	44.6%	21.8%	79%	
					NS		NS						
Ghi	III	261	70 Gy, 35	(TPF)=>cisplatin/5-FU x 2				48%		38.2%*	13.7%*	23%~	
		160		(TPF)=>cetuximab				43%		36.1%*	19.6%*	38%~	
									NS		p < 0.001		
(CC)RT or (CC)RT + anti-EGFR													
Concert-1	II	63	70 Gy, 35	cisplatin 100 mg/m ² x 3	68% ^{oo} *	78% ^o		32%	27%	24%	13%	3%	51% ^{**}
Mesia		87		cisplatin 75 mg/m ² x 3 + panitumumab 9 mg/kg x 3	61% ^{oo} *	69% ^o		43%	40%	55%	31%	16%	61% ^{**}
RTOG 0522	III	447	72 Gy, 42 in 6 weeks or	cisplatin 100 mg/m ² x 2	80.1%	72.9%* ^{ooo}				57%	33%	15%	
Ang		444	70 Gy, 35, in 6 weeks	cisplatin 100 mg/m ² x 2 + cetuximab	74.1%	75.8%* ^{ooo}				53%	43%	25%	
					p = 0.97		p = 0.32		p = 0.002		p < 0.001		
NCIC CTG HN.6	III	156	70 Gy, 35 in 7 weeks	cisplatin 100 mg/m ² x 3		85% ^o	73%* ^o			32%	38%	33%	19% ^{~~~~}
Siu		159	70 Gy, 35 in 6 weeks	panitumumab 9 mg/kg x3		88% ^o	76%* ^o			31%	52%	14%	12% ^{~~~~}
									p = 0.83				
DAHANCA 19	III	309	66-68Gy, 2 Gy/fraction	cisplatin 40 mg/m ² /week in stage III/IV + nimorazole	73%* ⁺								
Eriksen		310	66-68Gy, 2 Gy/fraction	cisplatin 40 mg/m ² /week in stage III/IV + nimorazole + zalutumumab 8 mg/kg/week	71%* ⁺								
RT + anti-EGFR or CCRT + anti-EGFR													
GORTEC 2007-01	III	201	70 Gy, 35	cetuximab	61.2% ^{ooo}	54.9%	40.5%* ^{ooo}			61%	59%	14%/3% ^{***}	
Bourhis		204		cetuximab + carboplatin/5-FU x 3	78.4% ^{ooo}	60.8%	52.3%* ^{ooo}			73%	63%	15%/4% ^{***}	
					p = 0.0005		NS		p = 0.015				
ICT + RT + anti-EGFR or CCRT													
GORTEC 2007-02	III	179	70 Gy, 35	carboplatin/5-FU x 3	HR = 0.98	HR = 1.12	HR = 0.93*			50%	29%	13%/8% ^{***}	
Geoffrois		181		TPF x 3 => cetuximab						48%	53%	18%/3% ^{***}	
					p = 0.90		p = 0.39		p = 0.58				

Legenda

N: number of patients
LRC: locoregional control rate
n: number of fractions
Gy: Gray
RT: radiotherapy
NS: not significant

CCRT: chemoradiation
SAE: serious adverse events
carboplatin/5-FU: carboplatin 70 mg/m² + 5-fluorouracil 600 mg/m²/day, day 1-4
cisplatin/5-FU: cisplatin 20 mg/m²/day and 5-FU 800 mg/m²/day day 1-4

*: (co-)primary endpoint
**: modifications in cisplatin dose
***: interruption > 7 days/ permanent discontinuation
~: interruption > 3 consecutive days
~: RT completed 70 Gy

^o: at 2 years
^{oo}: dose modifications
^{ooo}: at 3 years
^{~~~~}: any interruption
⁺: at 4 years

Conclusions

- ✓ CCRT is superior to RT + anti-EGFR
- ✓ CCRT + anti-EGFR is superior to RT plus anti-EGFR
- ✓ CCRT + anti-EGFR is not superior to CCRT
- ✓ AFX (accelerated fractionation RT) + anti-EGFR is not superior to CCRT
- ✓ Non-inferiority has not been demonstrated.

CCRT is still the standard of care in patients with LA-HNSCC.

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