ARO 04-01

MITOMYCIN C VS WEEKLY CISPLATIN · CHEMORADIOTHERAPY

Cisplatin did not improve overall survival

Int J Radiat Oncol Biol Phys 2026, journal pre-proof · Budach et al.

DESIGN · PHASE III, SUPERIORITY

Final 10-year analysis

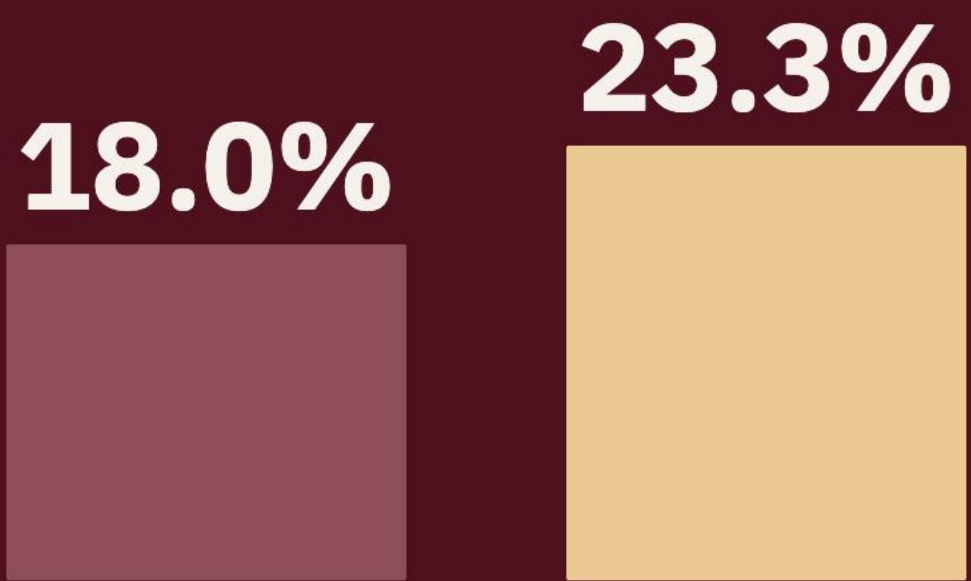
Randomised 1:1 | **2004–2008** | **Median 87 mo**

PATIENTS	364 randomised · unresectable stage IVA/IVB oropharynx or hypopharynx
BOTH ARMS	HART 72 Gy in 45 fractions over 6 weeks, with 5-FU
ARMS	MMC 10 mg/m² on days 5 and 36 vs CDDP 30 mg/m² weekly, up to 6 cycles
PRIMARY	Overall survival, intention to treat (182 vs 182)

HART: hyperfractionated accelerated RT · MMC: mitomycin C · CDDP: cisplatin

PRIMARY END POINT · KAPLAN–MEIER

Overall survival at 10 years



Adjusted HR 0.89 (95% CI 0.69 to 1.15)

Log-rank P=0.418 · 244 deaths · HR: cisplatin vs mitomycin C

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SECONDARY END POINTS

Distant metastasis and progression

	MMC	CDDP
Distant metastasis at 5 years, competing risk sHR 0.66 (95% CI 0.45 to 0.96) · P=0.031	**36.1%**	25.9%
Progression at 5 years, competing risk sHR 0.73 (95% CI 0.55 to 0.98) · P=0.037	**56.3%**	45.6%
Free of distant metastasis at 10 years, Kaplan–Meier Adjusted HR 0.69 (95% CI 0.48 to 1.02) · P=0.060	**51.9%**	66.2%

- **Competing-risk analyses were post hoc and exploratory.**

HR, sHR (subdistribution): cisplatin (CDDP) vs mitomycin C (MMC)

SECONDARY END POINTS · 10 YEARS

Locoregional control did not differ

	MMC	CDDP
Locoregional control	53.5%	54.2%
Local control Adjusted HR 1.01 · P=0.956	64.1%	61.5%
Regional control	72.5%	75.3%

- 49.6% of all deaths were not cancer-related.
- Second malignant neoplasms: 12.6% vs 9.9%.

MMC: mitomycin C · CDDP: cisplatin · Kaplan–Meier estimates · HR: cisplatin vs mitomycin C

SAFETY

More adverse events with cisplatin

	MMC	CDDP
Adverse or serious adverse events, any grade 28 vs 44 of 182 patients · P=0.048	15.4%	24.2%
Mean serum creatinine, mg/dL During treatment · P<0.001	0.76	0.87
Thrombocytopenia, grade 2 or higher P=0.13	2.8%	6.7%

- Grade 3 acute dysphagia, mucositis and skin erythema were common in both arms; late effects did not differ.

MMC: mitomycin C · CDDP: cisplatin

LIMITATIONS

A trial initiated in 2004

1 Neither arm is a current standard: 5-FU and HART in both arms, weekly cisplatin 30 mg/m² (cumulative 180 mg/m²).

2 HPV/p16 status was not tested at entry; a retrospective result exists for 48% of evaluable cases.

3 The distant-control result is post hoc and exploratory. The trial was registered retrospectively in 2026.

HART: hyperfractionated accelerated radiotherapy · 5-FU: 5-fluorouracil

INTERPRETATION

> With accelerated radiotherapy and 5-FU, weekly cisplatin did not improve overall survival over mitomycin C. A post hoc analysis showed fewer distant metastases with cisplatin, which was also associated with more adverse events. The trial does not compare either regimen with single-agent cisplatin and conventional fractionation.

REFERENCE

Budach V, Werner J, Wittlinger M, et al. Mitomycin C/5-Fluorouracil Versus Cisplatin/5-Fluorouracil With Hyperfractionated Accelerated Radiotherapy in Locally Advanced Head and Neck Cancer: The ARO 04-01/AHMO Trial. Int J Radiat Oncol Biol Phys 2026; journal pre-proof. doi:10.1016/j.ijrobp.2026.10.060. DRKS00040575.

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Educational content for healthcare professionals. Not medical advice. Produced with AI assistance; figures checked against the full text.

Final 10-year analysis of the trial.

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