Nimotuzumab in Cervical Cancer

Updates on the current evidences

Innokeys

CIMaHer ™
nimotuzumab 50 mg

CIMaHer Product Profile

Brand Name	**CIMaHer**
Composition	Vial contain: Nimotuzumab 50 mg
Dosage Form	Injection
Manufacturer	Centro De Inmunologia Molecular (CIM), La Habana, Cuba
Mechanism of Action	Anti EGFR

Nimotuzumab (Indonesia)

Cervical Cancer: Treatment Options

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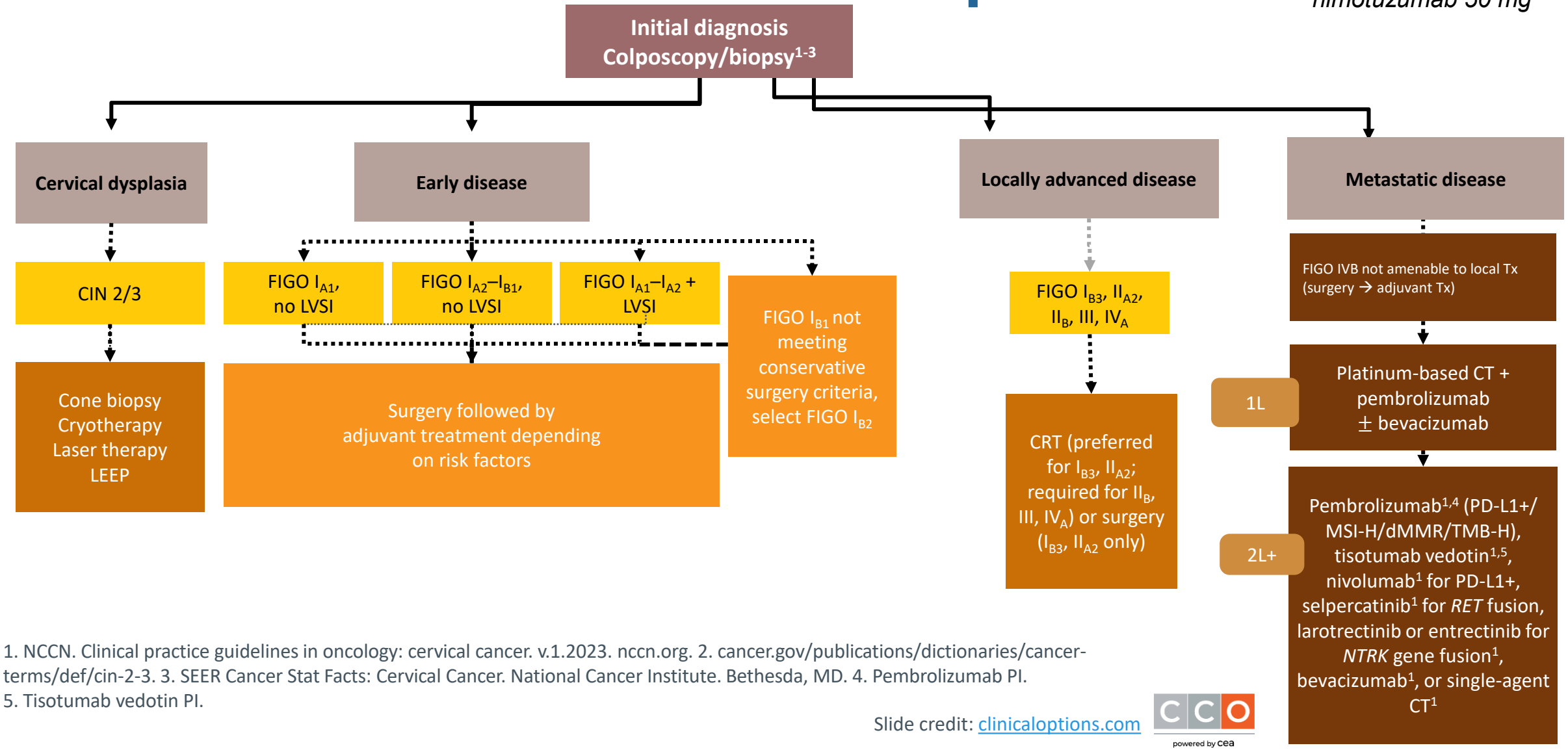

1. NCCN. Clinical practice guidelines in oncology: cervical cancer. v.1.2023. nccn.org. 2. cancer.gov/publications/dictionaries/cancer-terms/def/cin-2-3. 3. SEER Cancer Stat Facts: Cervical Cancer. National Cancer Institute. Bethesda, MD. 4. Pembrolizumab PI.
5. Tisotumab vedotin PI.

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NCCN Guidelines Version 1.2023
Cervical Cancer

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SYSTEMIC THERAPY FOR CERVICAL CANCER[a]

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	First-line Therapy[b,c]	Second-line or Subsequent Therapy[g]
Preferred Regimens • Cisplatin • Carboplatin if patient is cisplatin intolerant	**Preferred Regimens** • Pembrolizumab + cisplatin/paclitaxel ± bevacizumab for PD-L1–positive tumors (category 1)[d,e,f,1] • Pembrolizumab + carboplatin/paclitaxel ± bevacizumab for PD-L1–positive tumors (category 1)[d,e,f,1] • Cisplatin/paclitaxel/bevacizumab[d,2] (category 1) • Carboplatin/paclitaxel/bevacizumab[d] **Other Recommended Regimens** • Cisplatin/paclitaxel (category 1)[3,4] • Carboplatin/paclitaxel[5,6] (category 1 for patients who have received prior cisplatin therapy) • Topotecan/paclitaxel/bevacizumab[d,2,7] (category 1) • Topotecan/paclitaxel[7] • Cisplatin/topotecan[7] • Cisplatin[4] • Carboplatin[8,9]	**Preferred Regimens** • Pembrolizumab for TMB-H tumors[e,h] or PD-L1–positive or MSI-H/dMMR tumors[e,f,10] • Tisotumab vedotin-tftv[11] **Other Recommended Regimens** • Bevacizumab[d] • Paclitaxel[9,12] • Albumin-bound paclitaxel • Docetaxel • Fluorouracil • Gemcitabine • Pemetrexed • Topotecan • Vinorelbine • Irinotecan (category 2B) **Useful in Certain Circumstances** • Nivolumab for PD-L1–positive tumors[e,f,13] • Selpercatinib for RET gene fusion-positive tumors • Larotrectinib or entrectinib for *NTRK* gene fusion-positive tumors (category 2B)

Limited Treatment Options for LA-Cervical Cancer

Other molecules have been tested in combination with chemoradiation to treat Locally Advanced Cervical Cancer, but didn't reach significant clinical efficacy

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RTOG 0417 Trial

Bevacizumab + Cisplatin + RT
Vs
Cisplatin + RT

Result: Similar result with RTOG 9001 that compare CCRT vs RT

CC: Fluorouracil + Cisplatin

OUTBACK Trial

Cisplatin + RT
vs
Cisplatin + RT + adjuvant CT

ACT: Carboplatin + Paclitaxel

Result:
ACT didn't improve OS and PFS

CALLA Trial

Durvalumab + CRT
Vs
CRT

Result:
Additional of Durvalumab didn't significantly improve the PFS

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Nimotuzumab combined with chemoradiotherapy for the treatment of cervical cancer: A meta-analysis of randomized controlled trials

Yan Yuan[1,2], Jiuzhou Chen[1,2], Miao Fang[1,2], Yaru Guo[1,2], Xueqing Sun[1,2], Dehong Yu[3], Yilong Guo[3]* and Yong Xin[1,2]*

[1]Department of Radiation, the Affiliated Hospital of Xuzhou Medical University, Xuzhou, China, [2]Department of Cancer Institute, Xuzhou Medical University, Xuzhou, China, [3]Department of Radiation, the Affiliated Pizhou Hospital of Xuzhou Medical University, Xuzhou, China

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Journal:

frontiers | Frontiers in Oncology

H-Index: 102

Quartiles: Q1 (from 2013)

Total 6 studies (n=393) were analyzed

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Study	Study design	Sample size (Exp/Con)	Stage	Age/years		Nimotuzumab dose	Radiotherapy		chemotherapy
				Exp	Con		Radiotherapy types	Target area and radiation dose	
Cao Y 2019 (20)	RCT	46/46	IIb-IVa	55.43 ± 10.10	57.08 ± 9.91	200mg/week/6 weeks	IMRT	Pelvic radiotherapy: 50~55 Gy Intracavitary radiotherapy: 5Gy/week	Cisplatin: 40mg/m^2/week/ 6 weeks
Chen YF 2015 (21)	RCT	36/36	IIb-IVa	54.2 ± 11.8	55.2 ± 11.5	200mg/week	IMRT	Pelvic radiotherapy: average dose:54.5 Gy Intracavitary radiotherapy: 5Gy/week/4-5 weeks	Nedaplatin: 40 mg/m^2/week
Sun MH 2020 (22)	RCT	37/37	Ib3-IVa	18~75	18~75	400mg/week/6 weeks	IMRT	Pelvic radiotherapy: 50.4 Gy Intracavitary radiotherapy: 30 Gy	Cisplatin: 40mg/m^2/week/ 6 weeks
Tian LC 2021 (23)	RCT	27/27	IIb-IV	54.80 ± 2.13	54.19 ± 2.07	200mg/week	IMRT	Pelvic radiotherapy: 45~50.4 Gy	Cisplatin: 40 mg/m^2/week
Yan HW 2021 (24)	RCT	21/20	III-IVa	49.31 ± 9.02	47.63 ± 8.79	100mg/week	IMRT	Pelvic radiotherapy: 50~55 Gy Metastatic lymph node: 59.92Gy Intracavitary radiotherapy	Paclitaxel: 135 mg/m^2/week Cisplatin: 75 mg/m^2/week
Zheng WT 2018 (25)	RCT	30/30	IIb-IV	49.52 ± 0.79	48.42 ± 0.58	200mg/week/6 weeks	NA	Pelvic radiotherapy: 50~55 Gy Metastatic lymph node:60Gy	Cisplatin: 40mg/m^2/week/ 6 weeks

RCT, randomized controlled trial; IMRT, intensity modulated radiation therapy; NA, not available.

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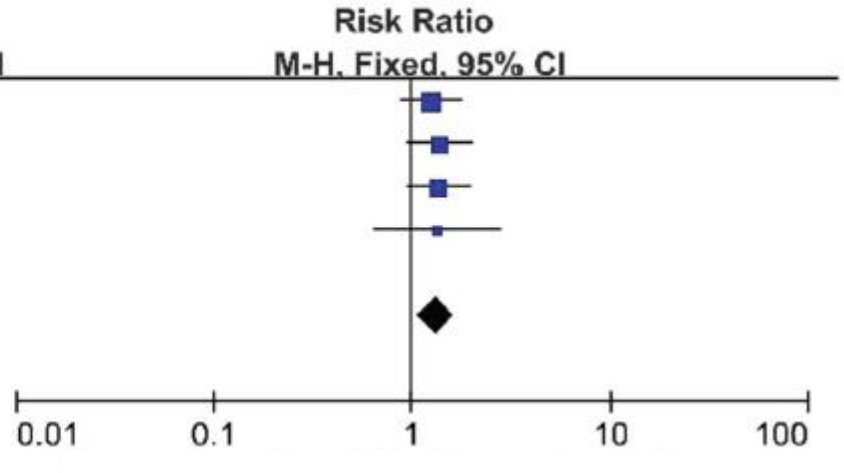
Complete Remission Rate (CRR): Disappearance of all target lesions

A

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cao Y 2019	29	46	23	46	34.2%	1.26 [0.88, 1.81]
Chen YF 2015	25	36	18	36	26.8%	1.39 [0.94, 2.06]
Sun MH 2020	26	37	19	37	28.3%	1.37 [0.94, 2.00]
Yan HW 2021	10	21	7	20	10.7%	1.36 [0.64, 2.87]
Total (95% CI)		**140**		**139**	**100.0%**	**1.34 [1.08, 1.65]**
Total events	90		67			

Heterogeneity: $Chi^2 = 0.15$, $df = 3$ ($P = 0.98$); $I^2 = 0\%$

Test for overall effect: $Z = 2.70$ ($P = 0.007$)



Additional of Nimotuzumab increase CRR by 34% (Significantly higher)

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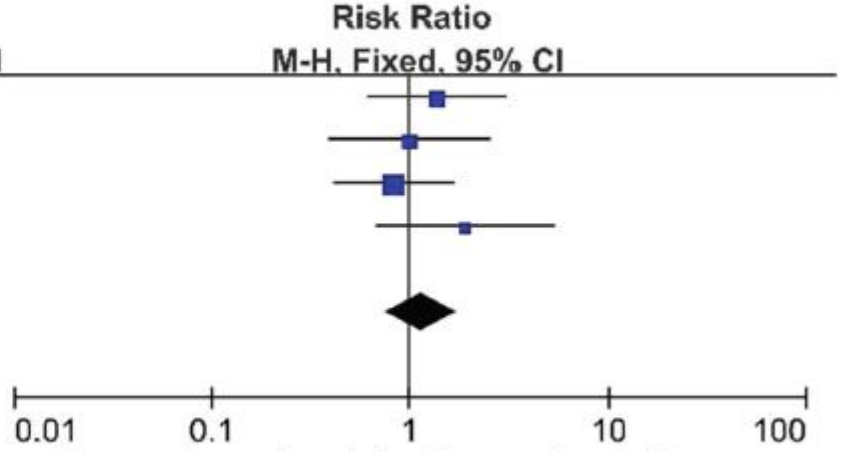
Partial Remission Rate (PRR): At least 30% reduction in the total diameter of the target lesion

B

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cao Y 2019	11	46	8	46	25.7%	1.38 [0.61, 3.10]
Chen YF 2015	7	36	7	36	22.5%	1.00 [0.39, 2.56]
Sun MH 2020	10	37	12	37	38.6%	0.83 [0.41, 1.69]
Yan HW 2021	8	21	4	20	13.2%	1.90 [0.68, 5.35]
Total (95% CI)		**140**		**139**	**100.0%**	**1.15 [0.76, 1.75]**
Total events	36		31			

Heterogeneity: Chi² = 1.99, df = 3 (P = 0.57); I² = 0%
Test for overall effect: Z = 0.66 (P = 0.51)



Additional of Nimotuzumab increase PRR by 15%
(Not statistically significant)

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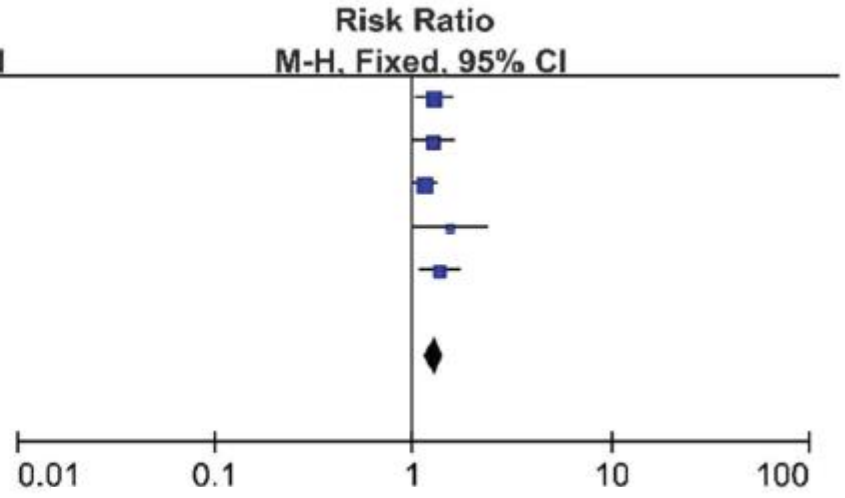
Objective Response Rate (PRR): The proportion of patients whose tumor shrunk to a certain extent and stayed for a certain length of time (including CR and PR)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cao Y 2019	40	46	31	46	26.0%	1.29 [1.03, 1.62]
Chen YF 2015	32	36	25	36	21.0%	1.28 [1.00, 1.64]
Sun MH 2020	36	37	31	37	26.0%	1.16 [1.00, 1.35]
Yan HW 2021	18	21	11	20	9.4%	1.56 [1.01, 2.40]
Zheng WT 2018	29	30	21	30	17.6%	1.38 [1.08, 1.76]
Total (95% CI)		**170**		**169**	**100.0%**	**1.30 [1.16, 1.44]**
Total events	155		119			

Heterogeneity: Chi² = 2.98, df = 4 (P = 0.56); I² = 0%
Test for overall effect: Z = 4.73 (P < 0.00001)



Additional of Nimotuzumab increase ORR by 30% (Significantly higher)

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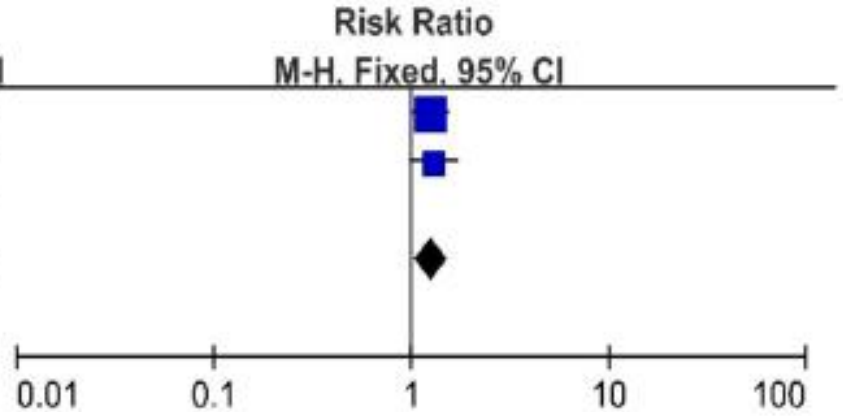
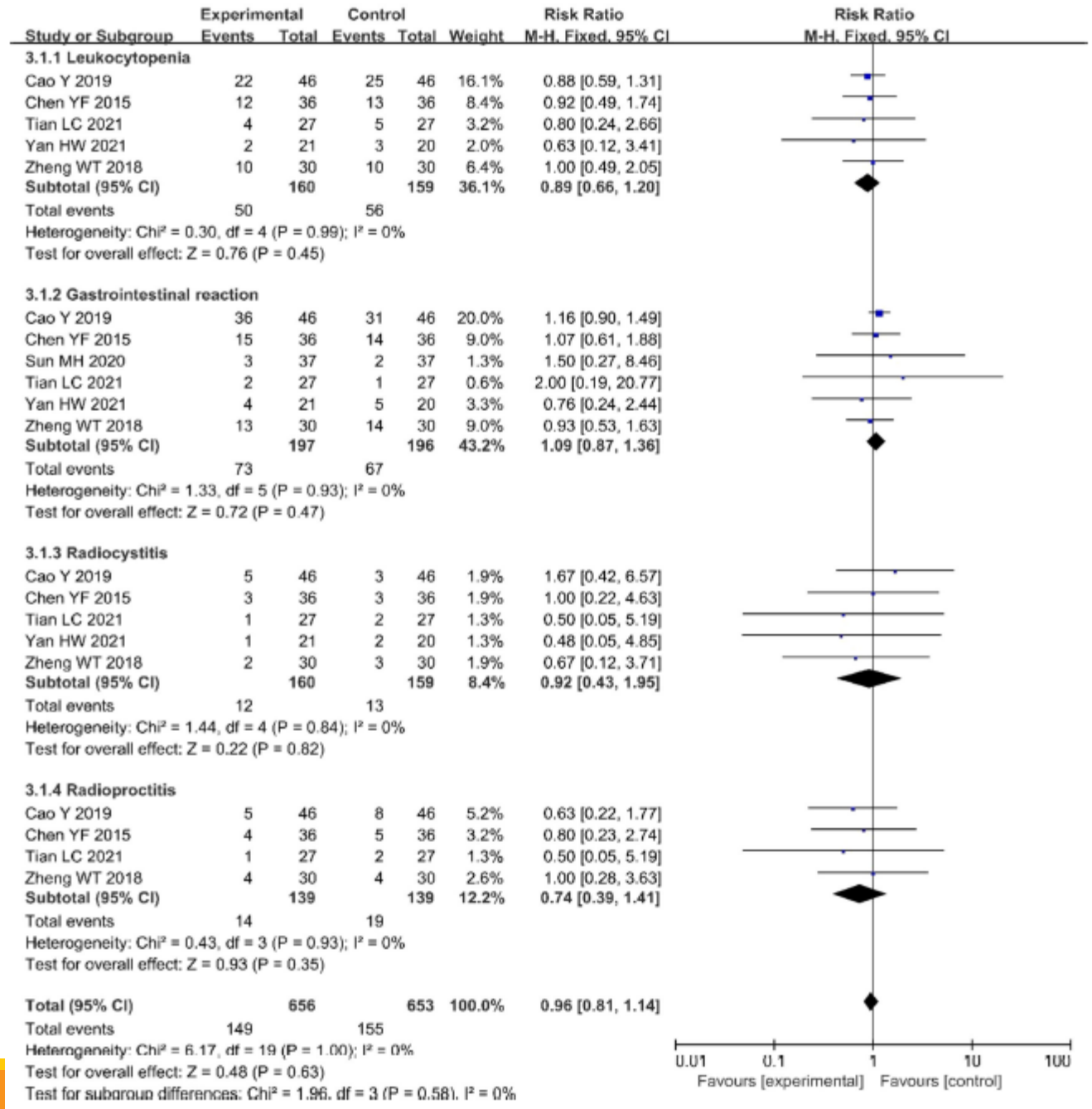
3-years of survival rates

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cao Y 2019	40	46	32	46	61.5%	1.25 [1.00, 1.56]
Zheng WT 2018	26	30	20	30	38.5%	1.30 [0.97, 1.74]
Total (95% CI)		**76**		**76**	**100.0%**	**1.27 [1.06, 1.51]**
Total events	66		52			

Heterogeneity: Chi² = 0.04, df = 1 (P = 0.83); I² = 0%
Test for overall effect: Z = 2.65 (P = 0.008)



Additional of Nimotuzumab increase 3-year survival rates by 27% (Significantly higher)



Side effects:

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Additional of Nimotuzumab didn't statistically significant increase the side effects

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Conclusions

- **Additional of Nimotuzumab in LACC significantly improve CRR, ORR and 3 year survival in Nimotuzumab combination group, compare with the CRT alone group.**
- **Additional of Nimotuzumab didn’t significantly increase side effects, compared with the CRT alone group.**

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Additional of Nimotuzumab are beneficial, combining with CRT

A pilot study of nimotuzumab plus single agent chemotherapy as second- or third-line treatment or more in patients with recurrent, persistent or metastatic cervical cancer

Lucely Cetina[1,2,8], Tania Crombet[3], Roberto Jiménez-Lima[1,8], Sergio Zapata[1], Mayra Ramos[3], Sandra Avila[1,8], Jaime Coronel[1,8], Eduardo Charco[1], Rafael Bojalil[2,4,8], Horacio Astudillo[2,5], Blanca Bazán[2,6], and Alfonso Dueñas-González[7,8,*]

[1]División de Investigación Clínica; Instituto Nacional de Cancerología, México City, México; [2]Doctorado en Ciencias Biológicas y de la Salud; Universidad Autónoma Metropolitana -Xochimilco, Ciudad de México; México City, México; [3]Centro de Inmunología Molecular, Habana, Cuba; [4]Instituto Nacional de Cardiología Ignacio Chávez; México City, México; [5]Hospital de Oncología, IMSS Siglo XXI; México City, México; [6]Instituto Nacional de Enfermedades Respiratorias; México City, México; [7]Unidad de Investigación Biomédica en Cáncer; Instituto de Investigaciones Biomédicas; UNAM/Instituto Nacional de Cancerología; México City, México; [8]On behalf of Tumor Study Group A.C., México City, Mexico

Keywords: advanced cervical cancer, EGFR, monoclonal antibody, nimotuzumab, pilot study

Abbreviations: ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; ECOG, Eastern Cooperative Oncology Group; EGFR, Epidermal Growth Factor Receptor; G-CSF, Granulocyte-Colony Stimulating Factor; RECIST, Response and Evaluation Criteria In Solid Tumors

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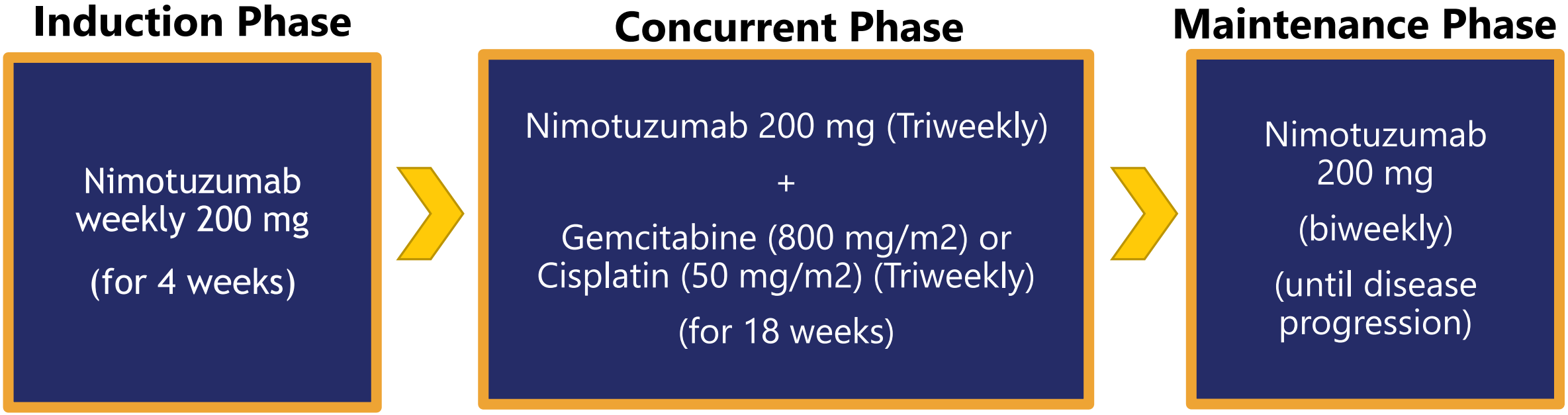
Study Design



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Results

- STABLE DISEASES WAS 35%
- MPFS = 163 DAYS
- MOS = 299 DAYS

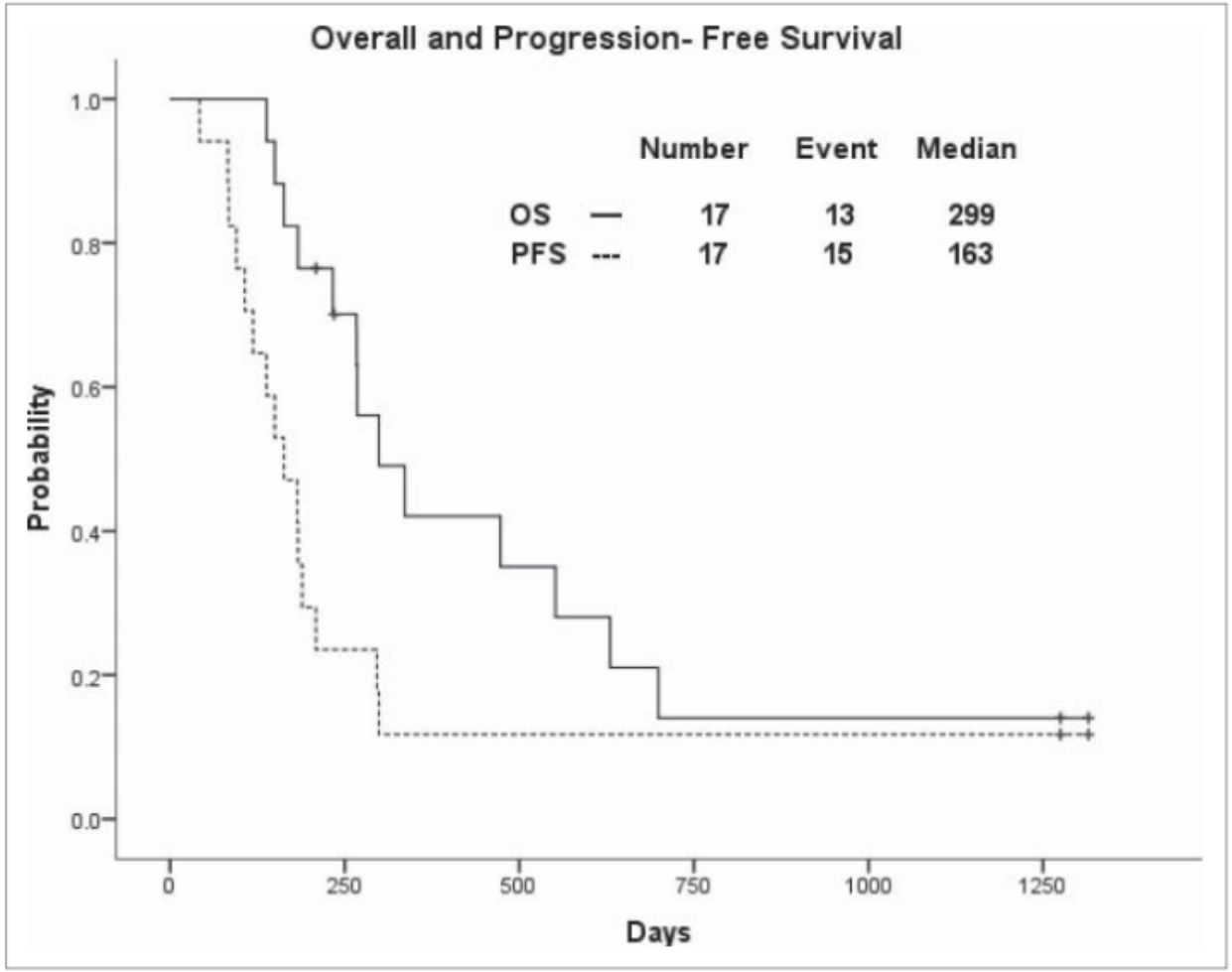

Figure 1. The median PFS and OS rates were 163 days (95% CI, 104 – 222), and 299 days (95% CI, 177–421).

Thank you