Cervical cancer: Current Therapy and Perspectives

"Global Access to Cancer Immunotherapy: Closing the Gaps"

Society for Immunotherapy of Cancer (SITC)

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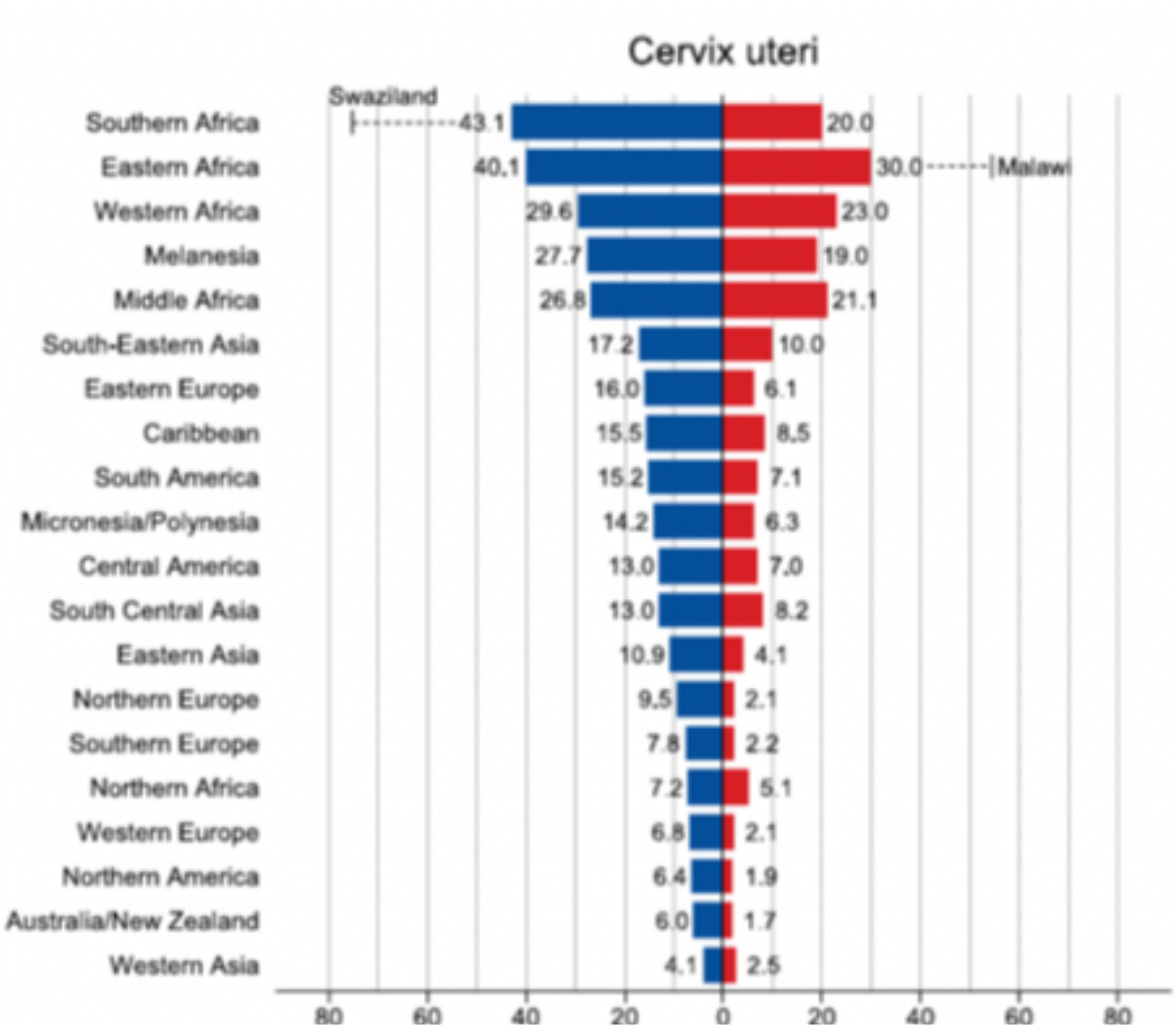
CERVICAL CANCER 2018 WORLWIDE

570 000
4th GLOBAL INCIDENCE

311 000
4th MORTALITY IN WOMEN



CURRENT TREATMENT GOALS

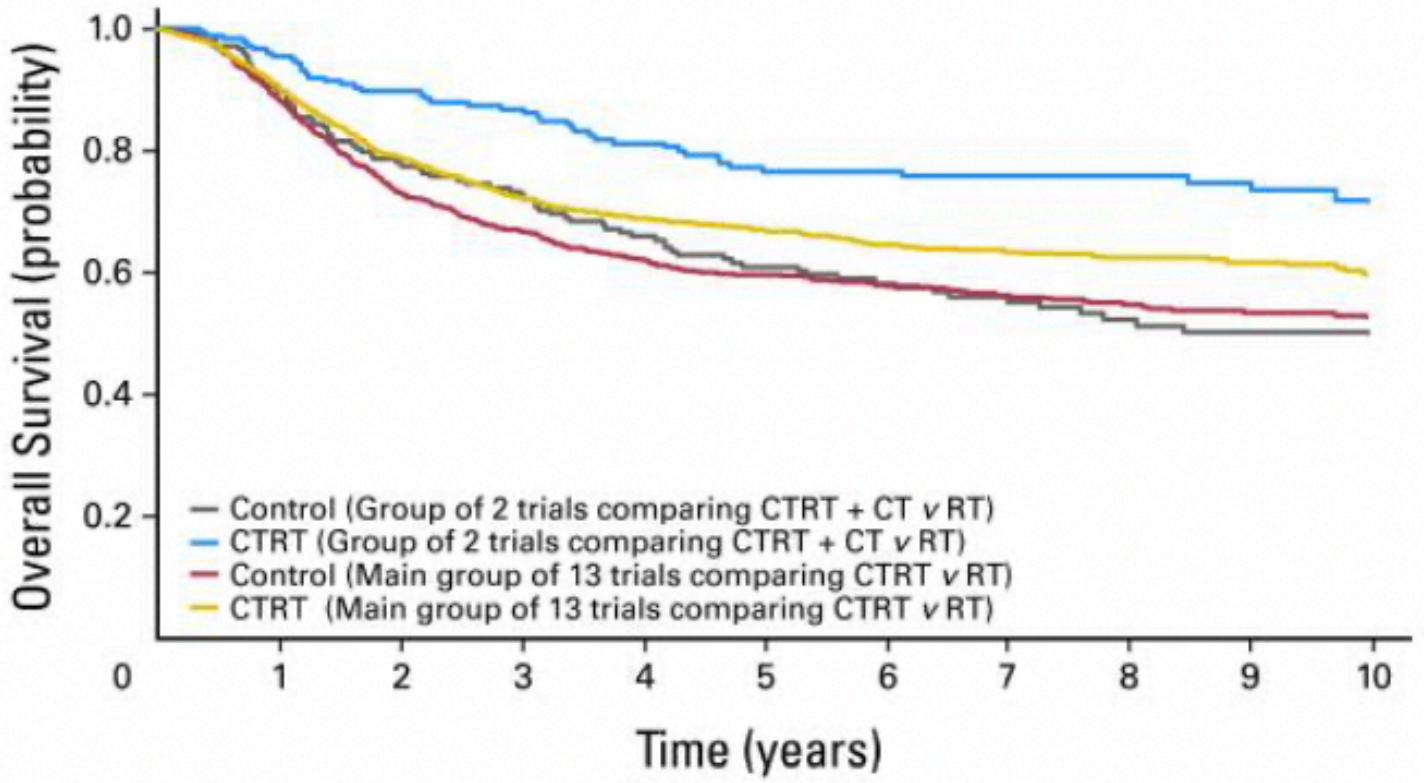
EARLY STAGES
cure/function preservation

LOCALY ADVANCED
cure

ADVANCED
palliation

• FIGO STAGES

- IA1, VERY EARLY
- LOCAL TREATMENT
- IA2, IB1, IIA1, EARLY
- SURGERY+CT-RT+ CHEMO
- IB2, IIA1, IIA2, IIB, IIIA,IIIB, IIIC, IVA. LOCALLY ADVANCED
- CT-RT
- IVB, RECURRENT PERSISTENT, ADVANCED
- CHEMO



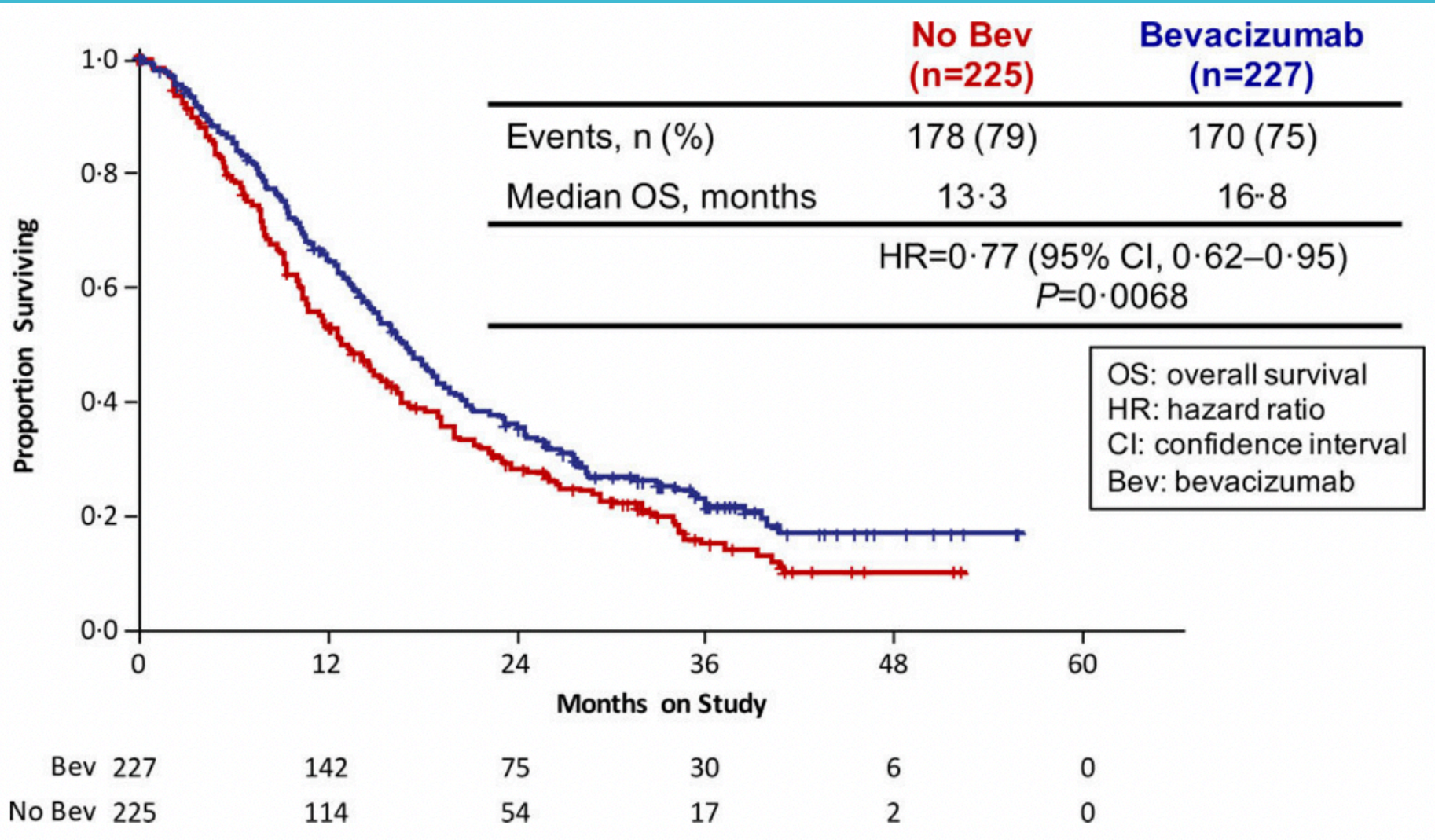
CISPLATIN CHEMO-RADIATION

Early disease &

Locally-advanced disease

TREATMENT OPTIONS FOR ADVANCED CERVICAL CANCER

- **Metastasic (IVB) or systemic recurrence** → **Palliative chemotherapy**
- **Local and/or systemic** → **Palliative Chemotherapy**
- **Local after Surgery** → **Chemoradiation**
- **Local after radiation**
  - **Central disease: (10%)** → **PE**
  - **Lateral disease (90%)** → **PE+IOP/RT** or **PRE-EXENT/QT**

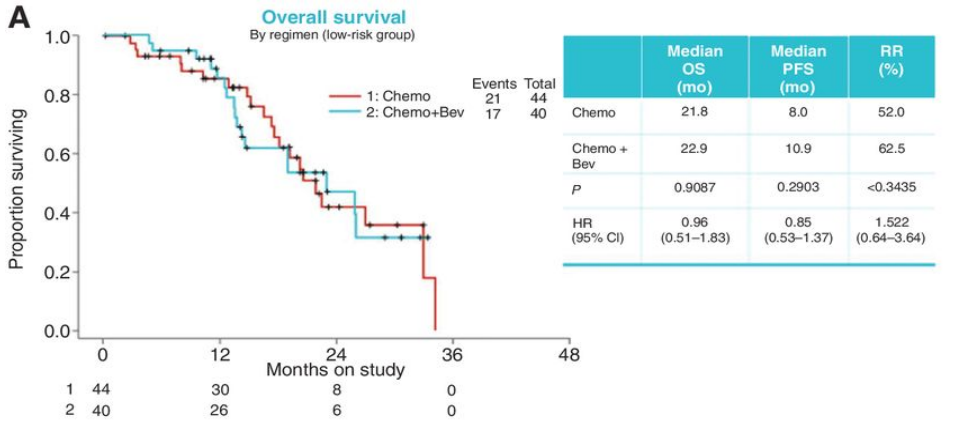


first-line
palliative
chemo

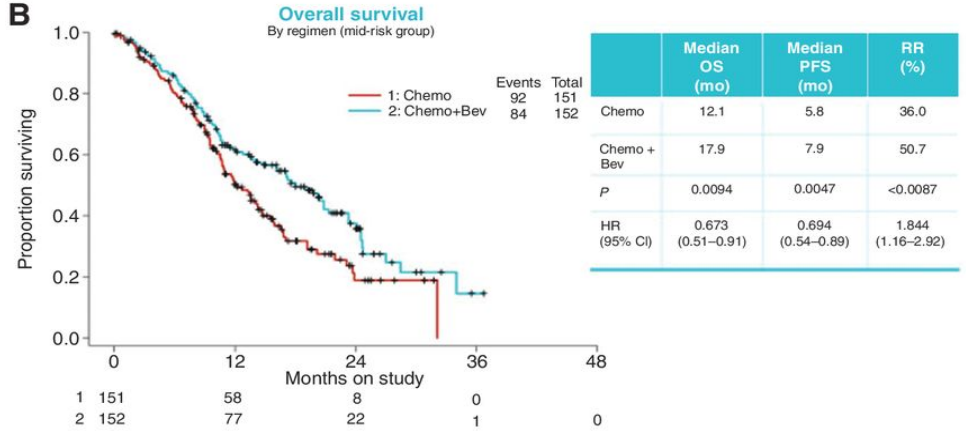
Overall Survival

Risk stratification

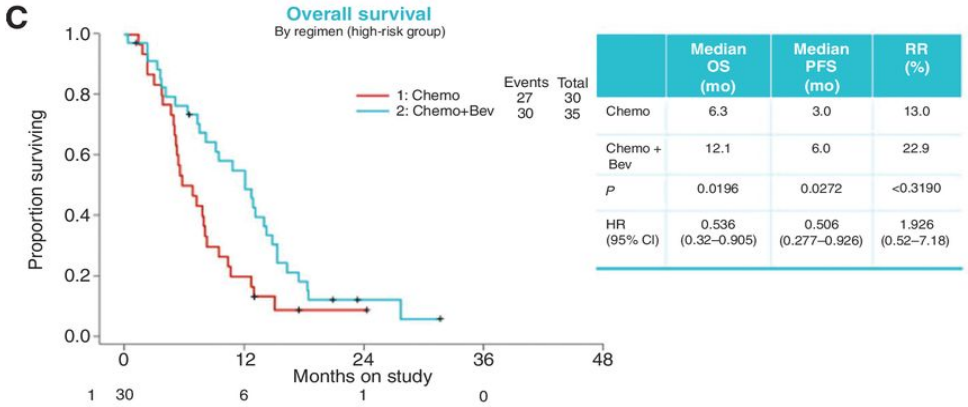
Moore criteria



	Median OS (mo)	Median PFS (mo)	RR (%)
Chemo	21.8	8.0	52.0
Chemo + Bev	22.9	10.9	62.5
P	0.9087	0.2903	<0.3435
HR (95% CI)	0.96 (0.51–1.83)	0.85 (0.53–1.37)	1.522 (0.64–3.64)



	Median OS (mo)	Median PFS (mo)	RR (%)
Chemo	12.1	5.8	36.0
Chemo + Bev	17.9	7.9	50.7
P	0.0094	0.0047	<0.0087
HR (95% CI)	0.673 (0.51–0.91)	0.694 (0.54–0.89)	1.844 (1.16–2.92)



	Median OS (mo)	Median PFS (mo)	RR (%)
Chemo	6.3	3.0	13.0
Chemo + Bev	12.1	6.0	22.9
P	0.0196	0.0272	<0.3190
HR (95% CI)	0.536 (0.32–0.905)	0.506 (0.277–0.926)	1.926 (0.52–7.18)

Krishnansu S. Tewari et al. Clin Cancer Res 2015;21:5480-5487

Second-Line palliative treatment
PEMBROZILUMAB

Nonrandomized phase Ib KEYNOTE-028 basket trial, 24 patients
RR 16.6% (zero complete and 4 partial responses)
NCCN category 2B

Nonrandomized phase II KEYNOTE-158 basket trial, 98 patients
RR 14.3% (3 complete and 9 partial responses).

NCCN Recategorized 2A option for patients with PD-L1–positive or MSI-H/dMMR tumors

RESEARCH IN PROGRESS FOR EARLY DISEASE

Randomized phase III trial (GOG-0263). FIGO STAGES I-IIA WITH INTERMEDIATE-RISK FACTORS

Adjuvant radiation
Vs.
Adjuvant chemoradiation

RANDOMIZED PHASE III (RTOG-0724). FIGO STAGES I-IIA WITH HIGH-RISK FACTORS

Adjuvant chemoradiation
Vs.
Adjuvant chemoradiation plus 4 cycles of carboplatin-paclitaxel

RESEARCH IN PROGRESS FOR LOCALLY ADVANCED DISEASE

INTERLACE. RANDOMIZED PHASE III TRIAL. IIB-IVA

Chemoradiation
Vs.
NACT Carboplatin-Paclitaxel 6 weekly cycles and then Chemoradiation

OUTBACK TRIAL. RANDOMIZED PHASE III TRIAL. IIB-IVA

Chemoradiation
Vs.
Chemoradiation followed by 4 cycles carboplatin paclitaxel

RESEARCH IN PROGRESS FOR LOCALLY ADVANCED DISEASE

TRIAPINE.RANDOMIZED PHASE III TRIAL. IIB-IVA
Chemoradiation
Vs.
Chemoradiation plus Triapine

NELFINAVIR.RANDOMIZED PHASE III TRIAL. IIB-IVA
Chemoradiation
Vs.
Chemoradiation plus Nelfinavir

ADX11 001. RANDOMIZED PHASE III TRIAL. IIB-IVA
Chemoradiation
Vs.
Chemoradiation plus ADX11 001

RESEARCH IN PROGRESS FOR ADVANCED DISEASE

Phase III (3 studies)

Chemo
Vs.
Chemo and pembrolizumab

Chemo
Vs.
Chemo and Atezolizumab

Chemo
Vs.
Chemo Prolgolimab

***Chemo**
Vs.
***Chemo and Cemiplimab**

SINGLE AGENTS AND COMBINATIONS NOT LONGER CONSIDERED

Table 1. Agents evaluated in cervical cancer showing insufficient activity and/or toxicity in phase I or phase II studies that have not proceeded to phase III trials.

Locally advanced stages
Erlotinib plus cisplatin/radiation
Cetuximab plus cisplatin/radiation
Panitumomab plus cisplatin/radiation
Sorafenib plus cisplatin/radiation
Everolimus plus cisplatin/radiation
Advanced disease
Lapatinib
Pazopanib
Imatinib
Cediranib
Brivanib
Sorafenib
Sunitinib
Temsirolimus
Erlotinib
Gefitinib
Cetuximab
Cetuximab plus cisplatin
Cetuximab plus cisplatin-topotecan
Nimotuzumab plus cisplatin-gemcitabine
Temsirolimus plus topotecan

OVERVIEW OF CPIs

HOW MANY CPIs ARE THERE?

ANTI-CTLA-4 (2)
Ipilimumab
Tremelimumab

ANTI-PD-1 (14)
Nivolumab
Pembrolizumab
Cemiplimab
Pidilizumab
JTX-4014
Spartalizumab
Camrelizumab
Sintilimab
Tislelizumab
Toripalimab
Dostarlimab
INCMGA00012
AMP-224
AMP-514

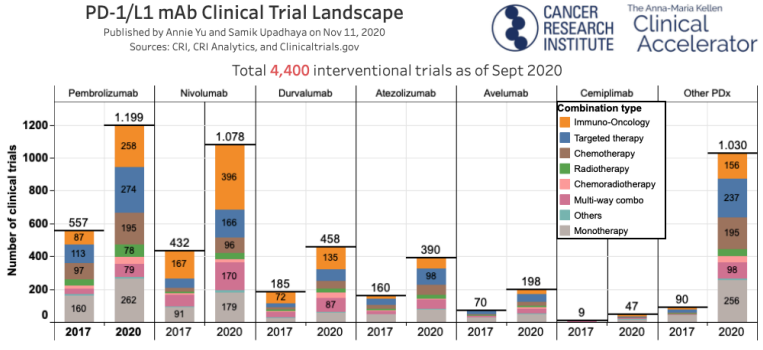
ANTI-PD-L1 (7)
Atezolizumab
Durvalumab
Avelumab
KN035
AUNP12
CA-170
BMS-986189

DO WE REALLY NEED MANY?

LOWER EFFICAY BAR
PLUS
HIGH-PRICED DRUGS

Incentive the pursuit of:
Marginal outcomes
Me-too mentality

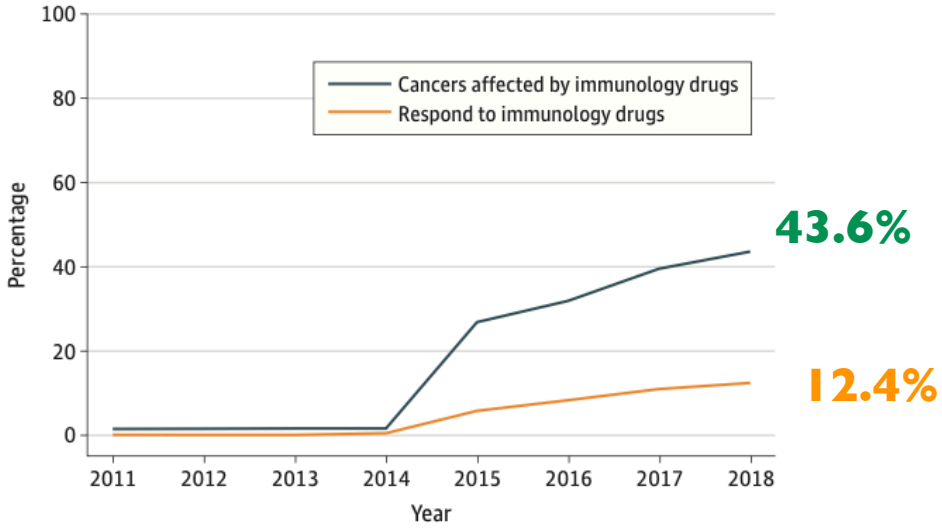
Which results on:
Duplication of effort and redundant pharmaceutical pipelines



INDUSTRY VISION OF THE CPI LANDSCAPE:
Visiongain has forecast that the overall global market for immune checkpoint inhibitors for cancer will be just over $16 billion in revenue by 2020.

ARE THEY EFFECTIVE? YES

Figure 1. Percentage of US Patients With Cancer Who May Benefit From and Respond to Checkpoint Inhibitor Immunology Drugs (2011-2018)



JAMA Network Open. 2019;2(5):e192535. doi:10.1001/jamanetworkopen.2019.2535

Trends in Cancer

CellPress
REVIEWS

Opinion

Hyperprogression and Immunotherapy: Fact, Fiction, or Alternative Fact?

406 pat (10 retrospective studies). Mean 31.8%, Median 15%

Outstanding Questions

Can we establish consensus criteria to define HPD?

Can prospective studies prove or disprove the HPD phenomenon?

What are the genomic signatures of HPD?

What are the immunologic signatures of HPD?

What are the surrogate markers of HPD?

Can patients be prospectively identified as being at risk of HPD?

Is it possible to establish management algorithms post disease progression?

Existing publication bias
98/4682 publications

Corporate control research proce
Funders set agenda
Control over study design & analsyis
Ownership of data

CONCLUSIONS

- Worldwide: cervical cancer remains the 4th cause of cancer incidence and mortality
- Early stages: Studies aim to optimize treatment in surgically treated
- Locally advanced: role of dose- dense NACT followed by CTRT, and Adj Chemo after CTRT
- Advanced: Chemo plus bevacizumab is the current standard of care for advanced disease
- Advanced: Ongoing phase III trials are testing immunotherapy added to chemo as first-line and second-line treatment for advanced disease.

CONCLUSIONS

- **CURRENT EVIDENCE POINTS TO THE EFFICACY OF CPIs FOR CERVICAL CANCER**
- **CERVICAL CANCER IS A DISEASE OF THE POOR COUNTRIES AND POOR WOMEN FROM RICH COUNTRIES**
- **GOVERNMENTS NEED TO COMMIT ON ESTABLISHING THEIR OWN AGENDAS FOR PROVIDE EFFECTIVE PREVENTIVE PROGRAMS AND TO SECURE RESOURCES FOR TREATING EVERY CASE OF INVASIVE DISEASE AS WELL.**
- **WHILE RESERCH MUST CONTINUE ON CPIs FOR CERVICAL CANCER, AS FOR TODAY THEIR AVAILABILITY FOR THIS DISEASE IS NOT A PRIORITY FROM THE PUBLIC HEALTH PERSPECTIVE**