

Adding 5 immunomodulators to radiotherapy and PD-1 blockade without further increasing financial toxicity: PRIMMO

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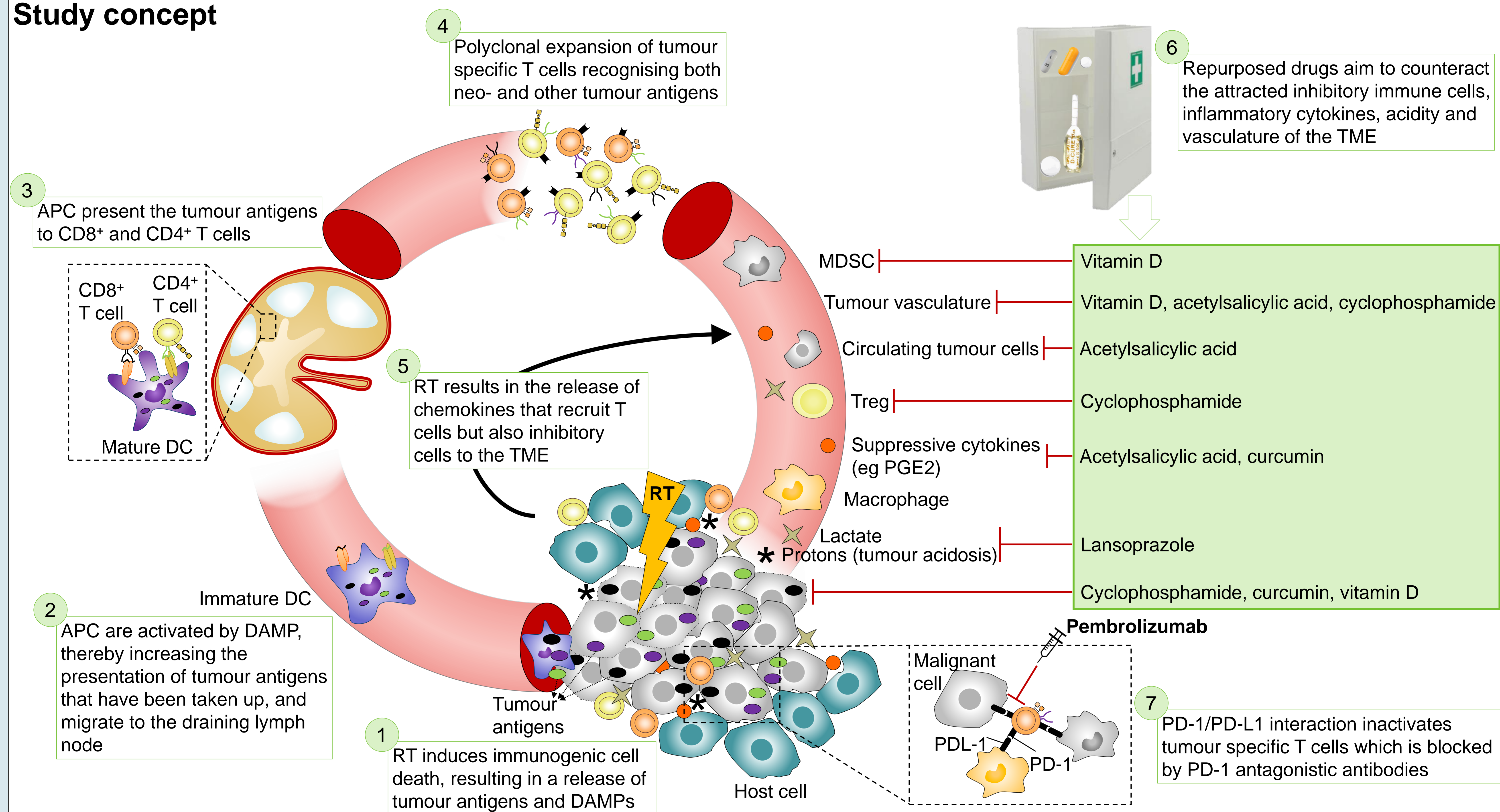
Background

- Tumour control will often require combination therapy.
- Combination of radiotherapy with dual checkpoint inhibition (CPI) improves survival in different mouse models and is currently in early phase clinical trial for gynaecological cancers (NCT03277482, NCT03452332).
- The launch price of novel anticancer drugs, including CPI, routinely exceeds 100 000 USD per year of treatment.
- Consequent financial toxicity brings the affordability of cancer care at stake for both patients and national healthcare services.
- We propose an alternative strategy allowing more immune modulation by combination therapy with repurposed drugs, metronomic chemotherapy and a food supplement: the PRIMMO trial (NCT03192059).

Objectives

- 1) Primary endpoint: objective response rate at week 26 according to immune related response criteria.
- 2) Secondary endpoints: safety, objective response rate at week 26 according to Response Evaluation Criteria in Solid Tumours, best overall response, progression-free survival, overall survival and quality of life.

Study concept



Study design & treatment schedule

Safety run-in N = 10	Endometrial cancer N _{total} = 25
	Cervical cancer N _{total} = 18
	Uterine sarcoma N = undefined

W1 W2 W3-4-5 W6-7-8 W9-10-11 W25

Day -14 Vitamin D (2000 IU)

Day -13 Vitamin D + curcumin (2 g)

Day -12 Vitamin D + curcumin + lansoprazole (180 mg uneven weeks; 30 mg even weeks)

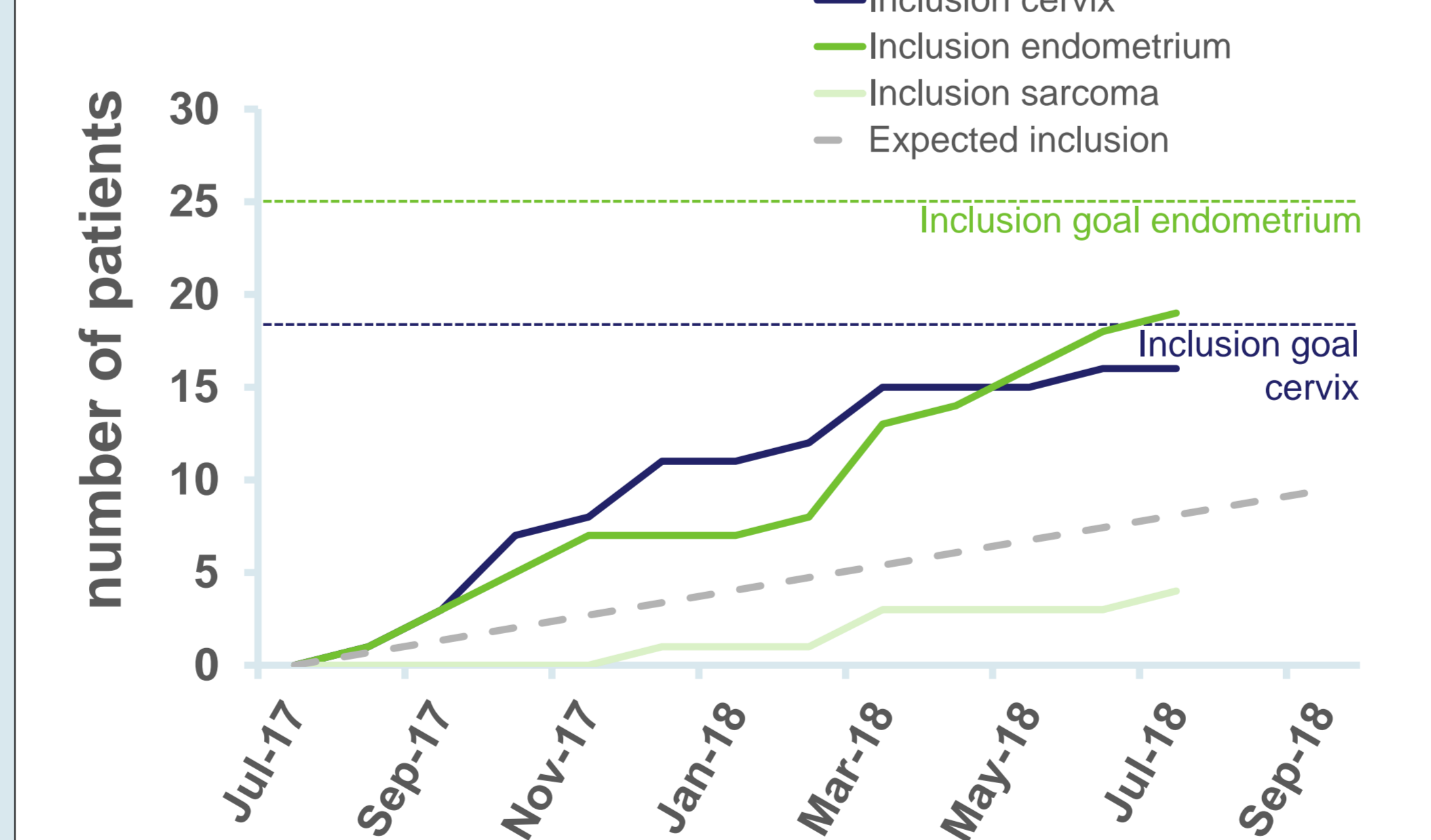
Day -11 Vitamin D + curcumin + lansoprazole + acetylsalicylic acid (325 mg)

Day -10 – w25 Vitamin D + curcumin + lansoprazole + acetylsalicylic acid + cyclophosphamide (50 mg)

Pembrolizumab 200 mg 6x q3w from day 1 (so W3, W6, W9, W12, W15 and W18)

Radiotherapy 3x 8 Gy, 48h apart (day 1, 3, 5)

Inclusion rate



Drug cost added to RT and α-PD-1

	PRIMMO*1	Dual CPI*1
Acetylsalicylic acid	23.22 €	-
Lansoprazole	186.48 €	-
Vitamin D	66.00 €	-
Cyclophosphamide	70.72 €	-
Curcumin	352.20 €	-
Ipilimumab	-	90 100 €
Total:	698.62 €	90 100 €

*1 Belgian prices obtained from www.bcfi.be and Farmaline for curcumin on January 2018

Conclusion

- Many existing drugs have an immune modulating potential and could therefore become repurposed for oncology. These are widely available and can be brought to patients fast.
 - PRIMMO trial:
 - 1) Patient inclusion goes faster than expected due to a better inclusion in each of the cohorts than anticipated.
 - 2) Multiple immune modulation with 5 repurposed drugs added to RT and α-PD-1 is much cheaper than dual checkpoint inhibition.
- The PRIMMO trial can inspire others to run investigator driven trials that explore the potential of combination treatments with drug repurposing to limit financial toxicity.**

More information

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