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OX40L+IL23+IL36γ (Triplet) (mRNA-2752)

Last updated: January 8, 2019

Modality	Program #	Program *Indication*	Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
Intratumoral immuno-oncology	mRNA-2416	OX40L *Solid tumors/lymphoma* *Ovarian carcinoma*					Worldwide
	mRNA-2752	OX40L+IL23+IL36γ *Solid tumors/lymphoma*					Worldwide
	MEDI1191	IL12 *Solid tumors*					50-50 U.S. profit sharing; AZ to pay royalties on ex-U.S. sales

mRNA-2752 has initiated dosing in a Phase 1 trial

OX40L+IL23+IL36γ (mRNA-2752) overview

- Moderna's technology enables novel combinations of targets
- Intratumoral delivery may enable delivery of targets locally that are too toxic systemically

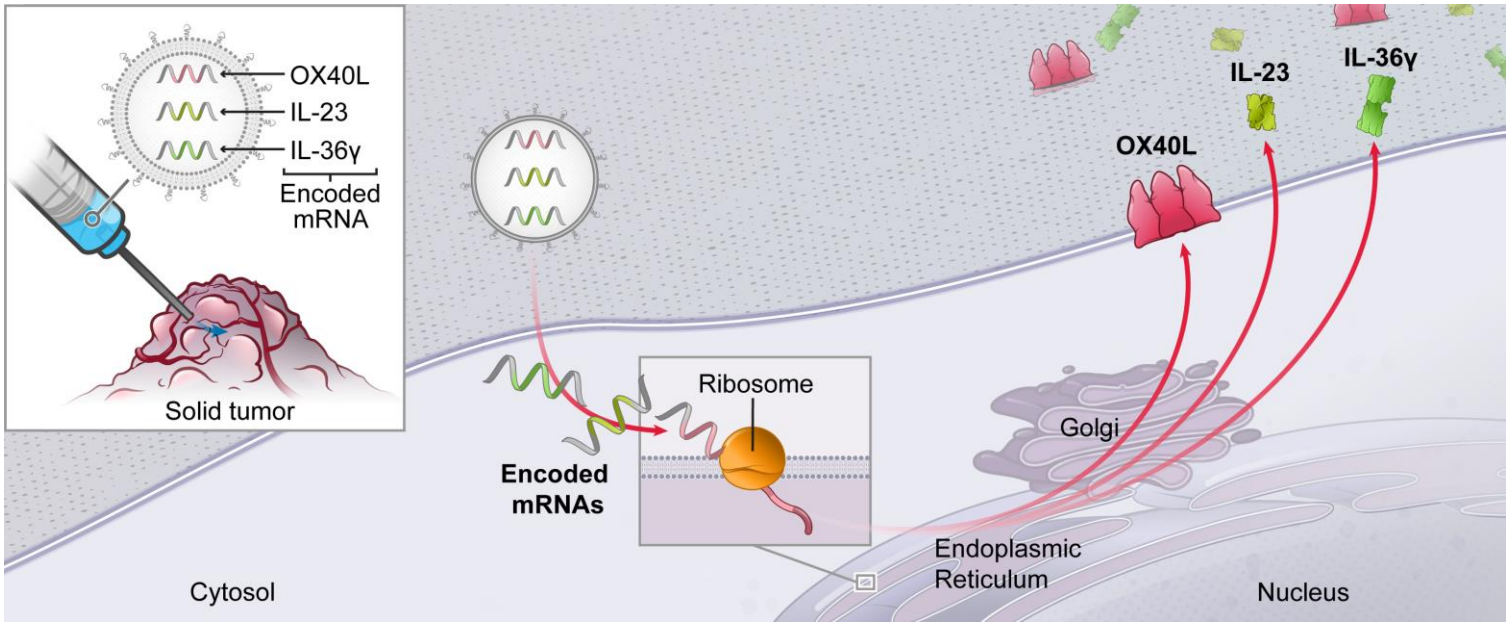
OX40L

- A **powerful co-stimulatory molecule** that enhances T cell expansion, function and memory formation
- **Native physiological conformation** (homotrimer membrane protein)

+

IL23 & IL36γ

- Have **established roles in mediating immune responses** and have been implicated in driving various inflammatory diseases
  - IL23 is a member of the IL12 family
  - IL36γ is a member of the IL1 family



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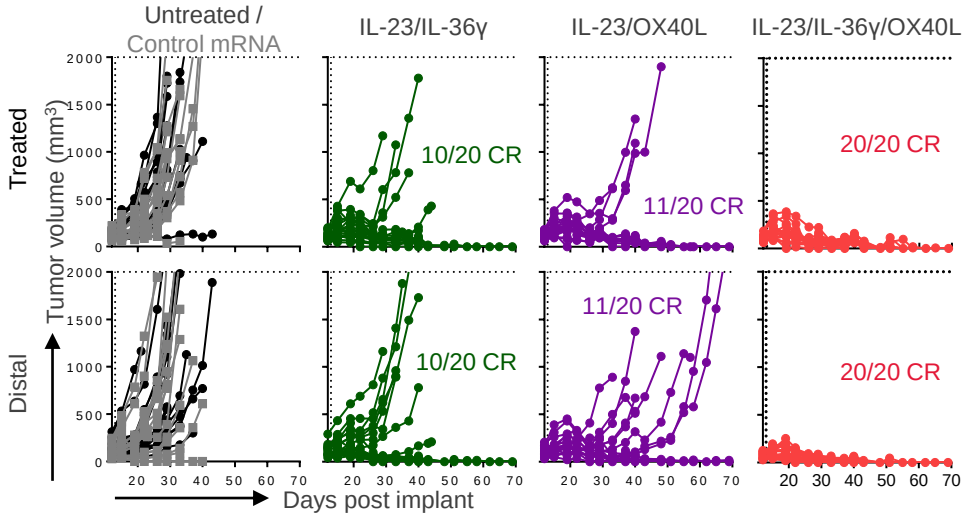
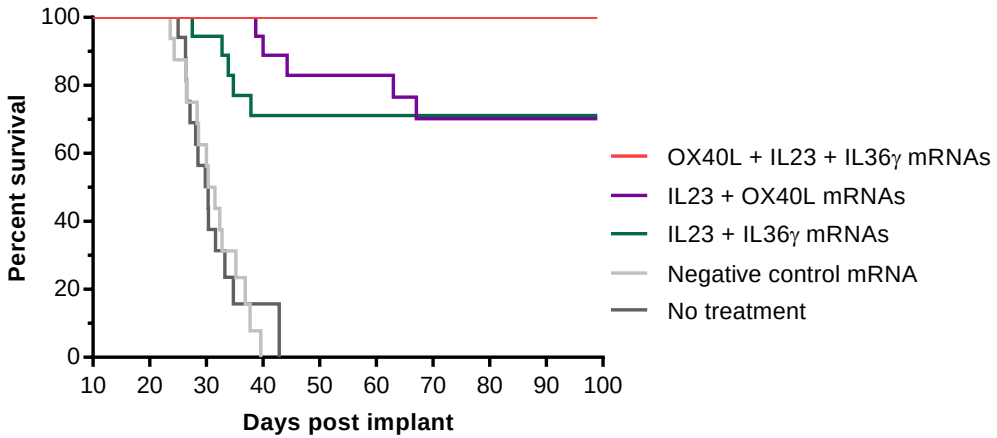
Pre-clinical data – combination demonstrates synergistic effects

Species: Mouse



Tumor volumes of both the treated and untreated tumors. Mice carrying bilateral MC38-S tumors received mRNA injected into the right flank tumor only.

Species: Mouse



100% (n=20) complete responders with mouse OX40L+IL23+IL36γ in MC38 dual flank syngeneic mouse model study

Regression of distal, untreated tumors following local treatment; 100% survival observed in pre-clinical studies

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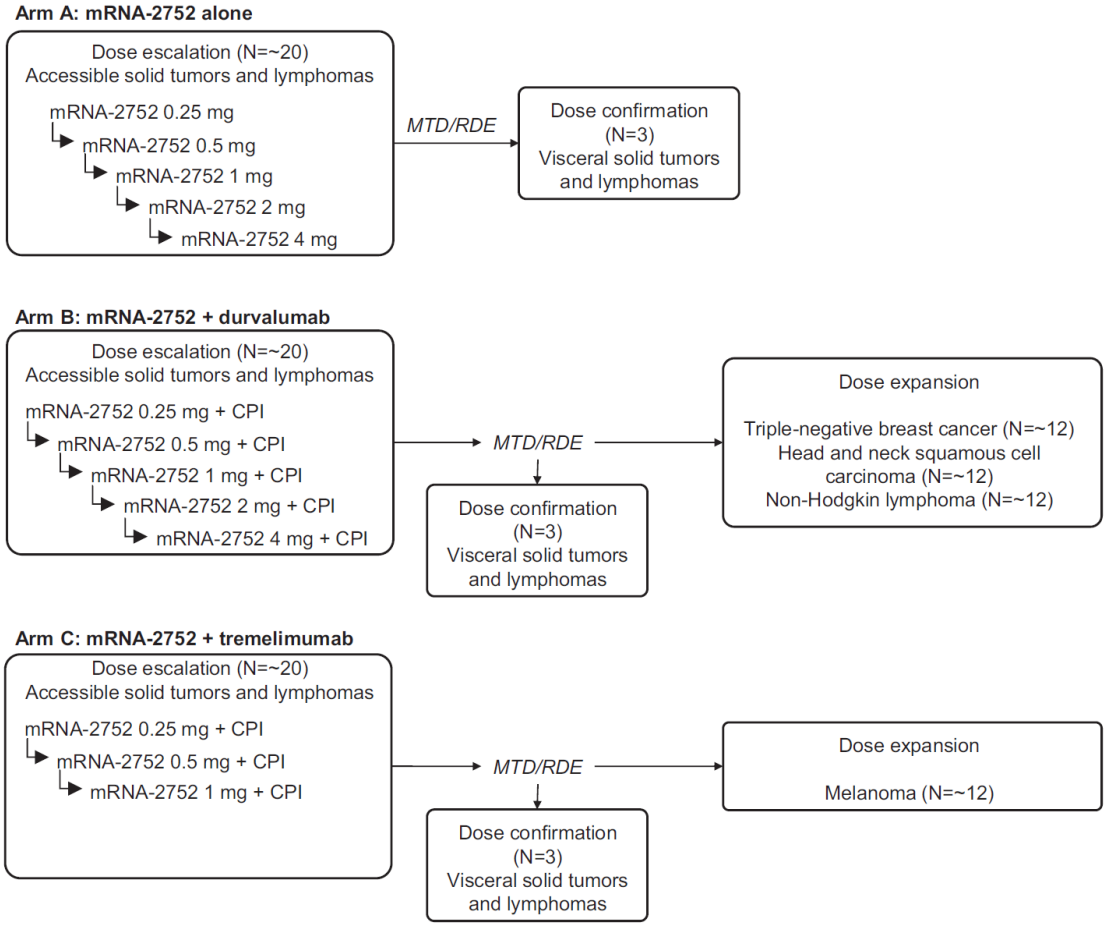
Phase 1 design

Key Objectives

- Evaluate safety and tolerability of mRNA-2752 administered alone and in combination with checkpoint inhibitors
- Define MTD and recommended dose for expansion for mRNA-2752 alone and in combination with checkpoint inhibitors
- Assess:
  - Anti-tumor activity
  - Protein expression in tumors
  - Pharmacokinetics
  - Assessment of immunological responses (exploratory)



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