



SITC 2017

November 8-12
NATIONAL HARBOR
MARYLAND

Gaylord National Hotel
& Convention Center



Society for Immunotherapy of Cancer

SITC
2017

Epigenetic Immunomodelling to Improve the Efficacy of Cancer Immunotherapy

Alessia Covre, PhD – *NIBIT Foundation*



#SITC2017

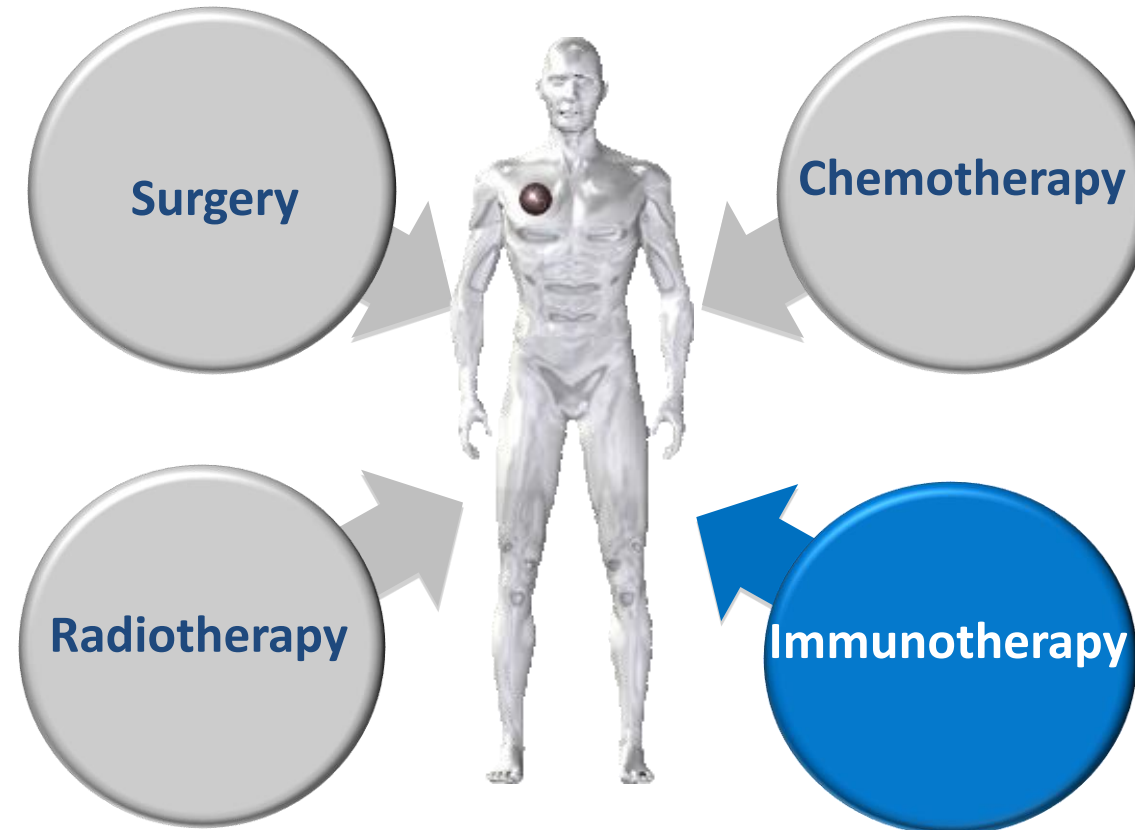
Presenter Disclosure Information

Alessia Covre

The following relationships exist related to this presentation:

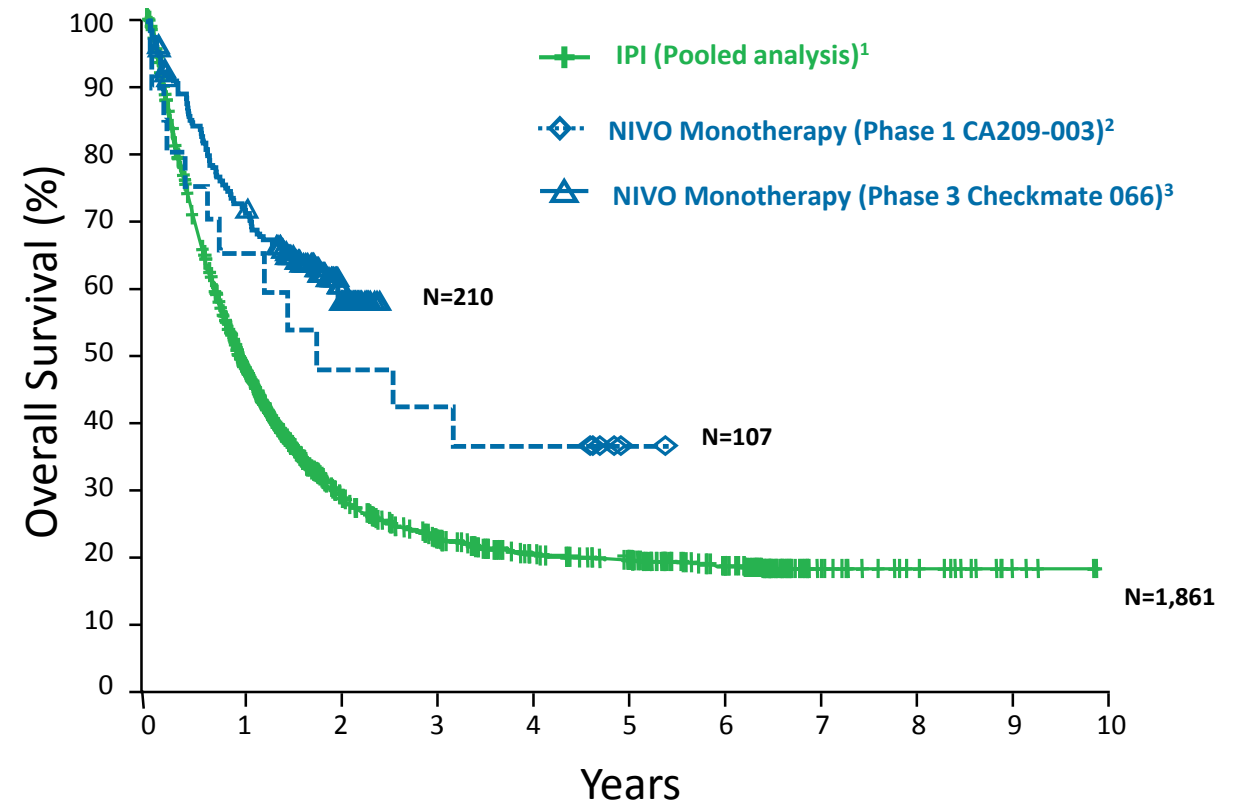
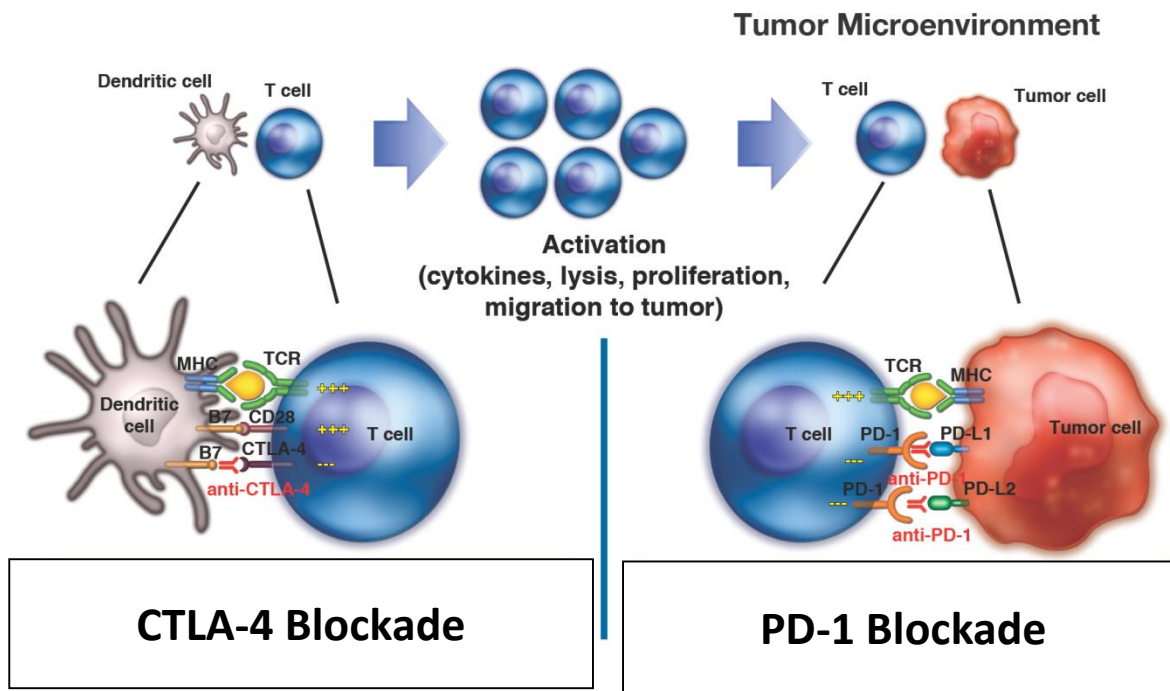
No Relationships to Disclose

Evolving Therapeutic Options for Cancer Treatment



ADVANCING CANCER IMMUNOTHERAPY WORLDWIDE

Immune Checkpoint Inhibitors Provide Durable Long-term Survival for Patients with Advanced Melanoma



1. Schadendorf et al. *J Clin Oncol* 2015;33:1889-1894;
2. Current analysis;
3. 3. Poster presentation by Dr. Victoria Atkinson at SMR 2015 International Congress.



New combo/sequences

Improve host's immune
system activity

HOST



Check-point mAb
CTA-based vaccines

COMBOS



Modulate
tumor immunogenicity
and immune recognition

TUMOR

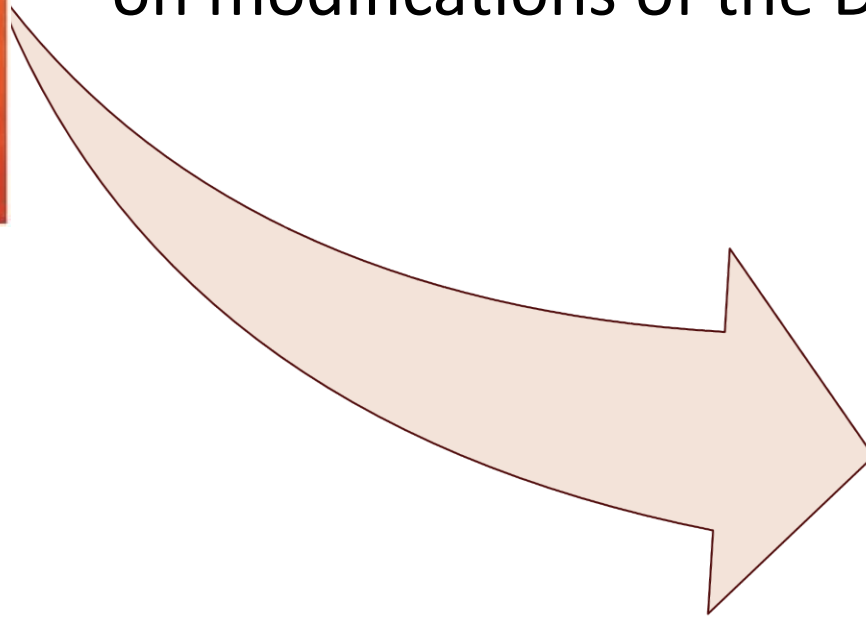


Epigenetic drugs

Epigenetics

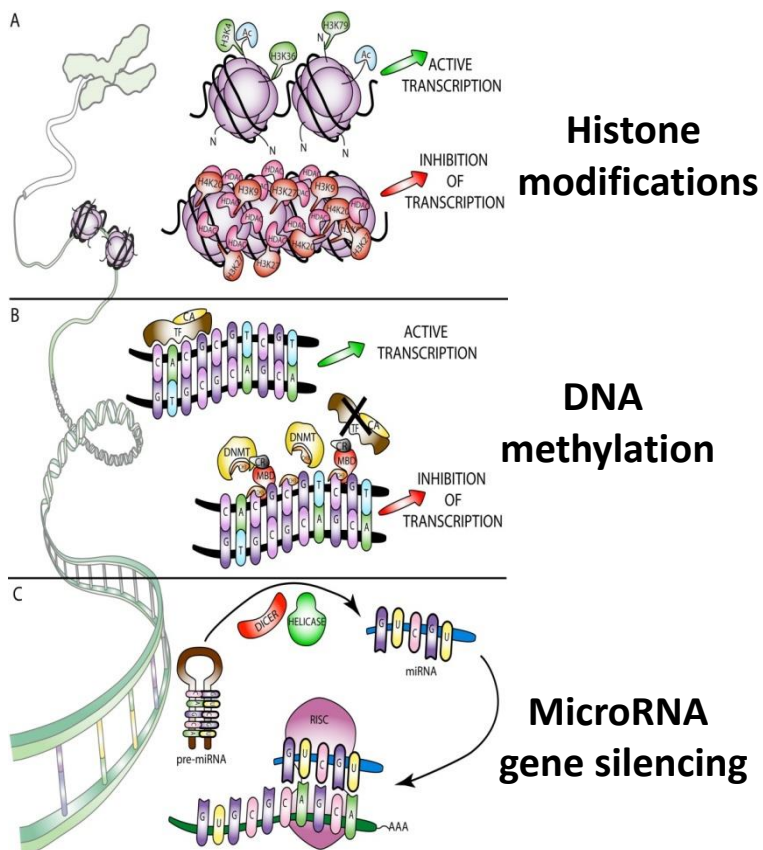


Heritable changes in gene expression
not based
on modifications of the DNA sequence



Epigenetics modifications

DNA hypomethylating agents

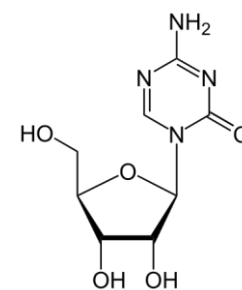


**PHARMACOLOGICALLY
REVERSIBLE**

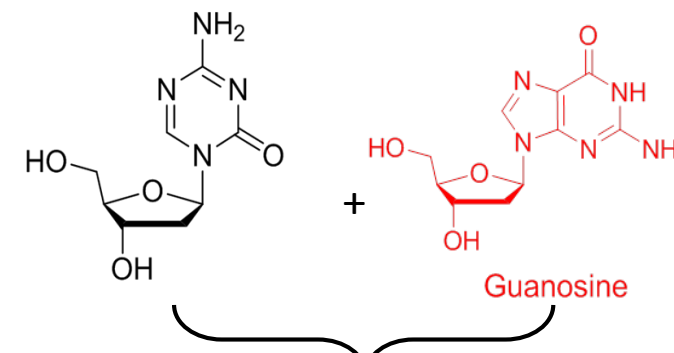
HDAC inhibitors
(HDACi)

DNMTs inhibitors
(DNMTi)

First generation

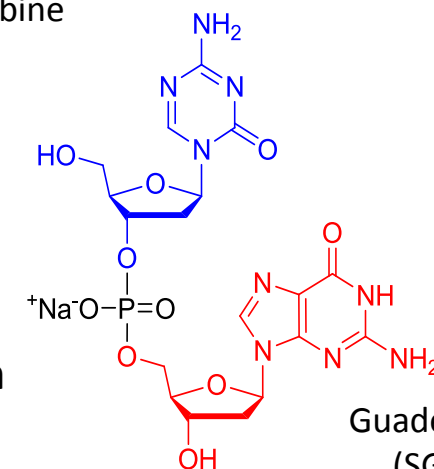


5'-Azacytidine



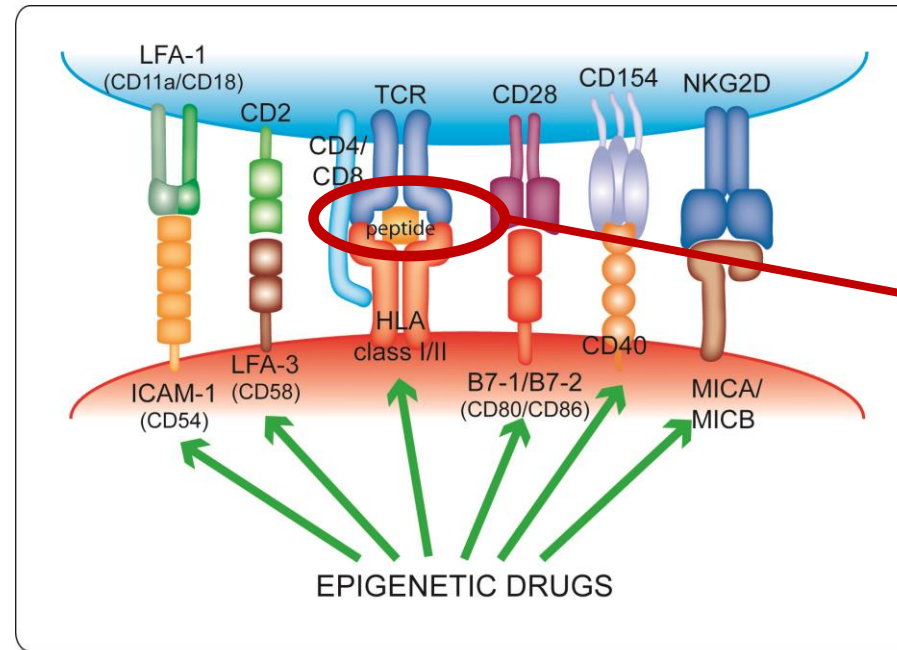
Decitabine

Next generation



Guadecitabine
(SGI-110)

Immune recognition



TAA peptide(s)

RESTORED/INCREASED
IMMUNE RECOGNITION
OF CANCER CELLS

L. Sigalotti et al. / Pharmacology & Therapeutics 2014



Melanoma immunomodulatory activities of DHAs

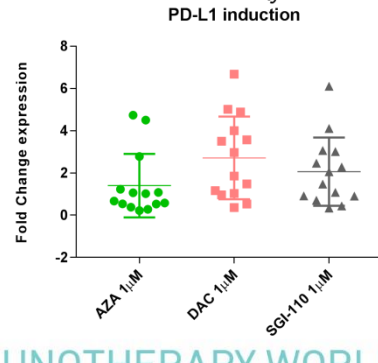
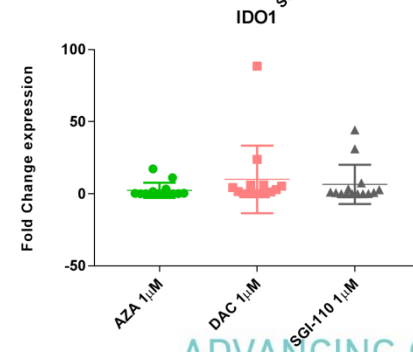
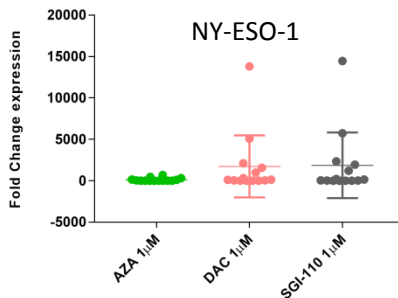
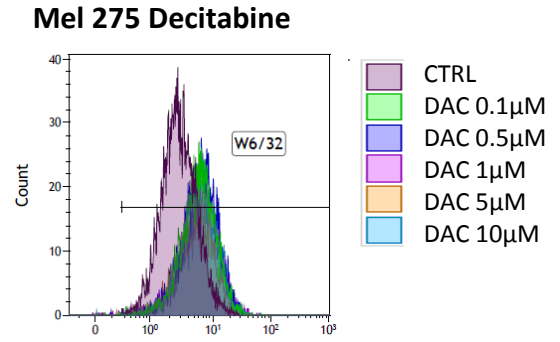
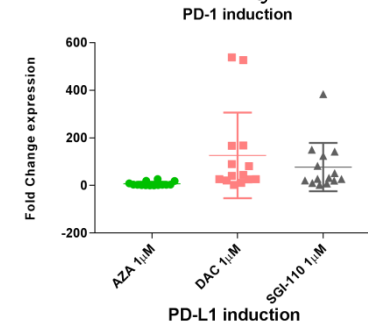
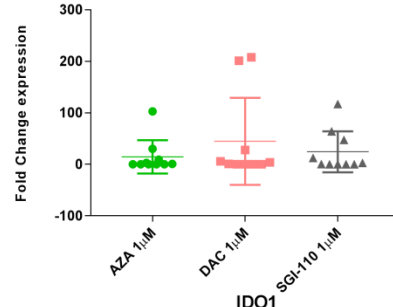
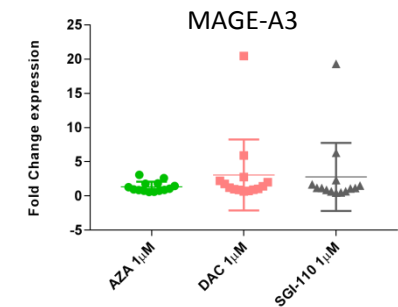
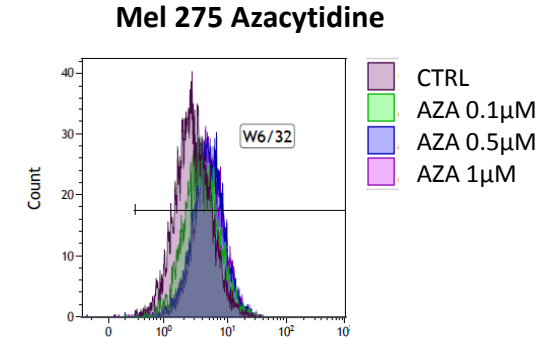
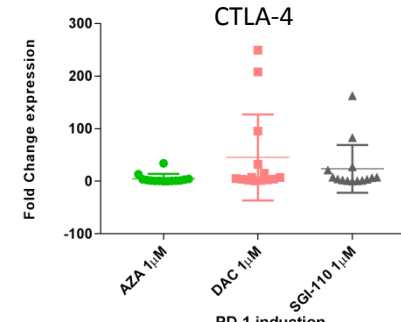
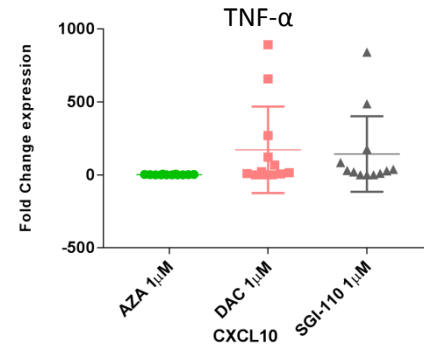
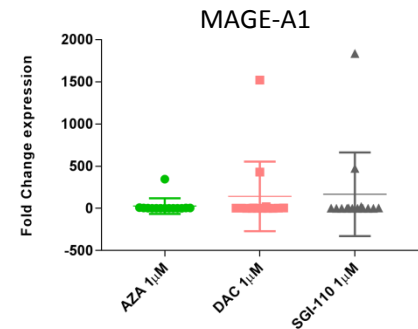


CTA

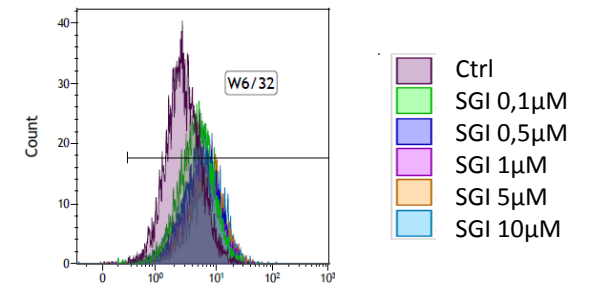
IMMUNOMODULATORS

IMMUNE CHECKPOINT

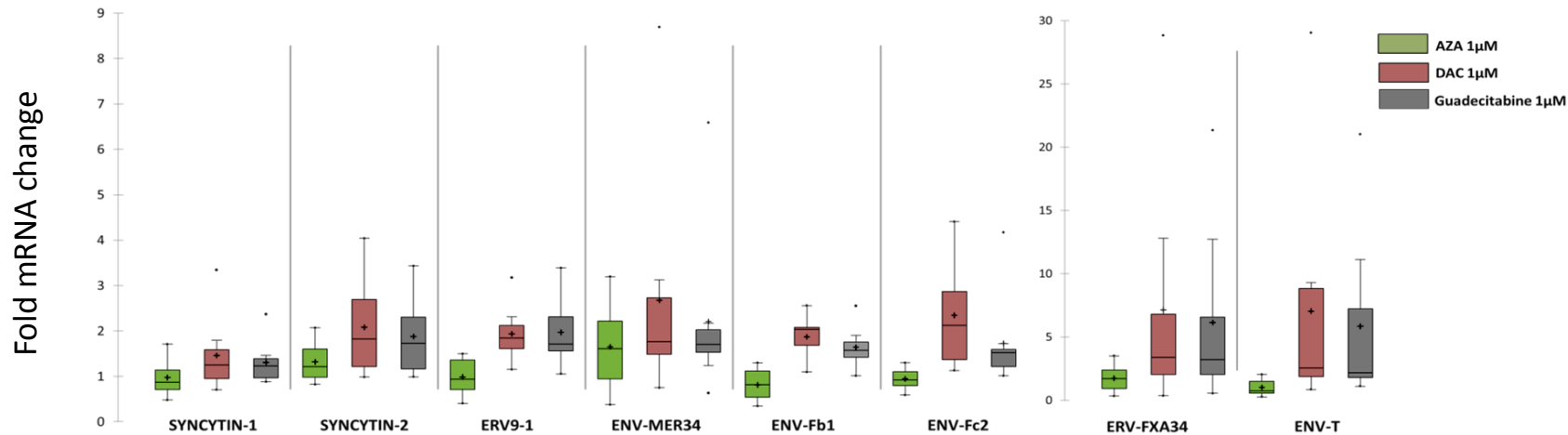
MHC classI



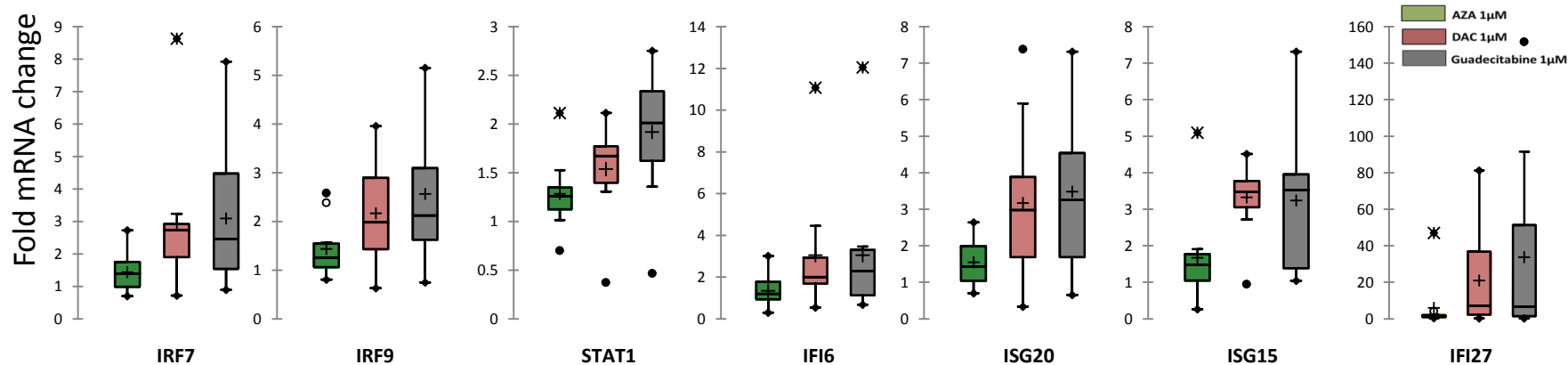
Mel 275 Guadecitabine (SGI-110)



Interferon stimulated genes modulation in melanoma cells by DHA

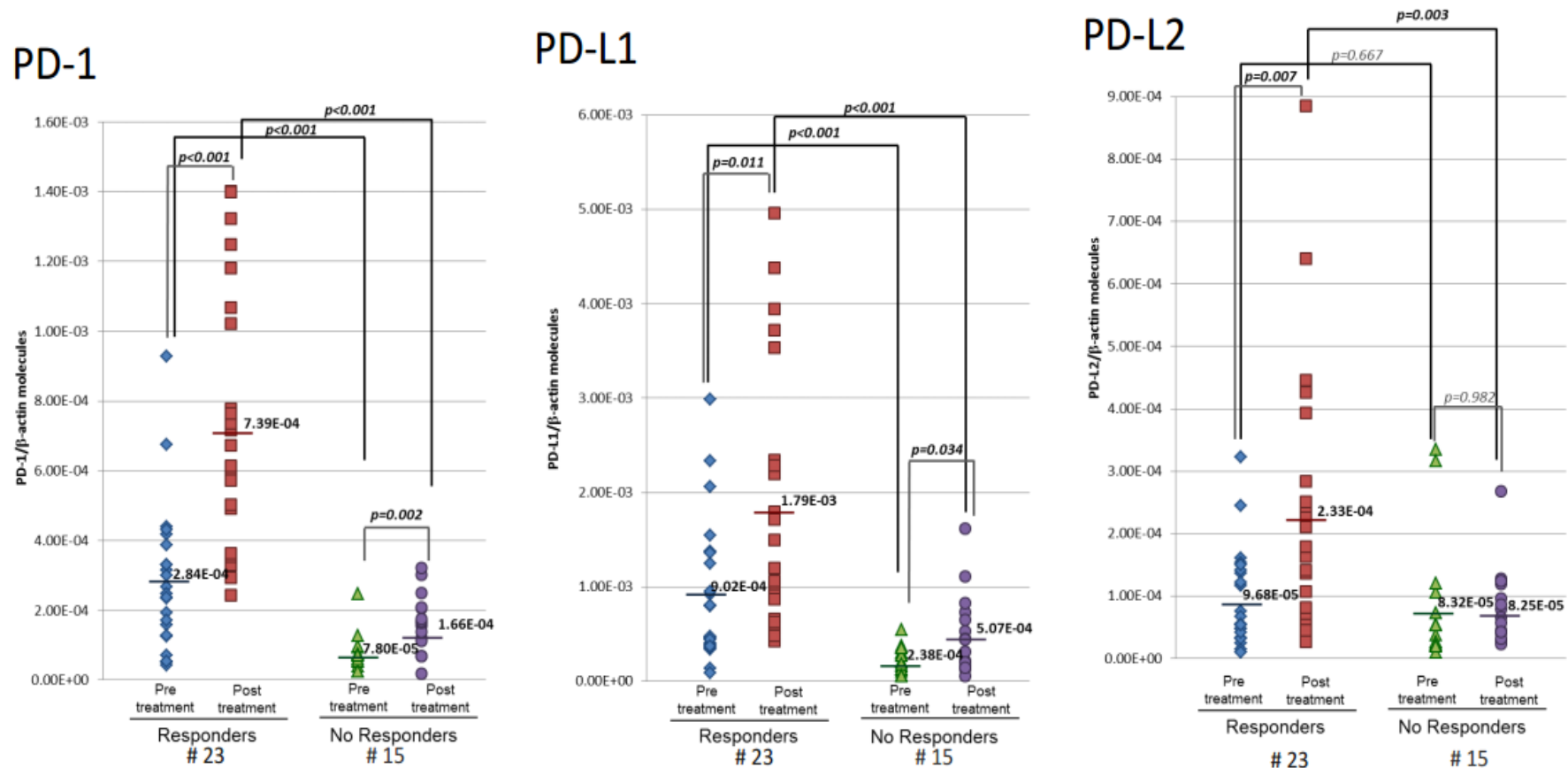


Endogenous retrovirus modulation in 8 human melanoma cell by DHA

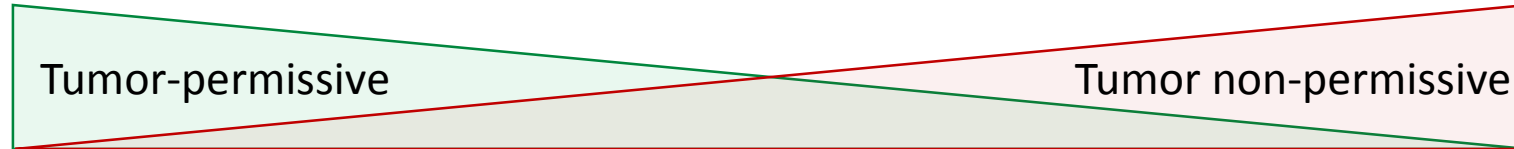


IFN pathway modulation in 10 human melanoma cell by DHA

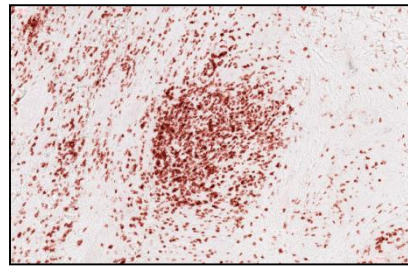
Regulation of Immune checkpoints expression in PBMC from AML patients by guadecitabine



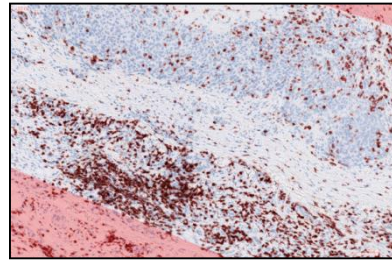
Tumor and TME phenotypes and immune response



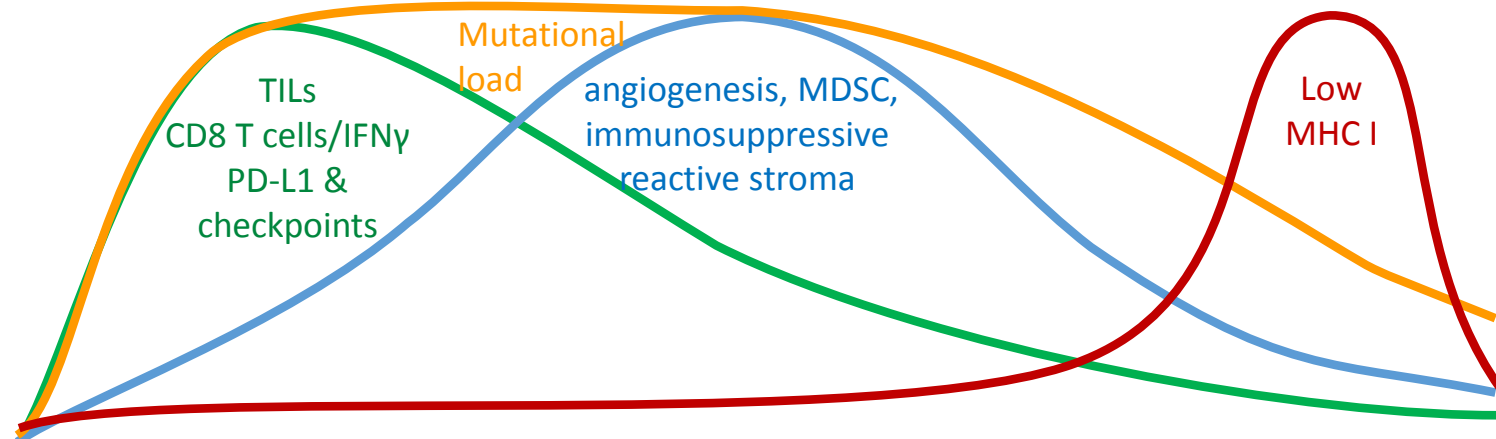
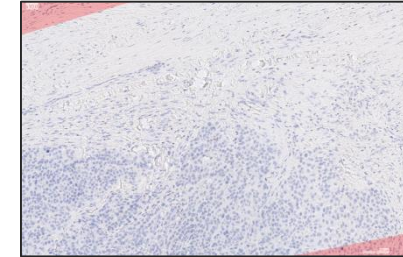
pre-existing immunity



T-cell migration defect

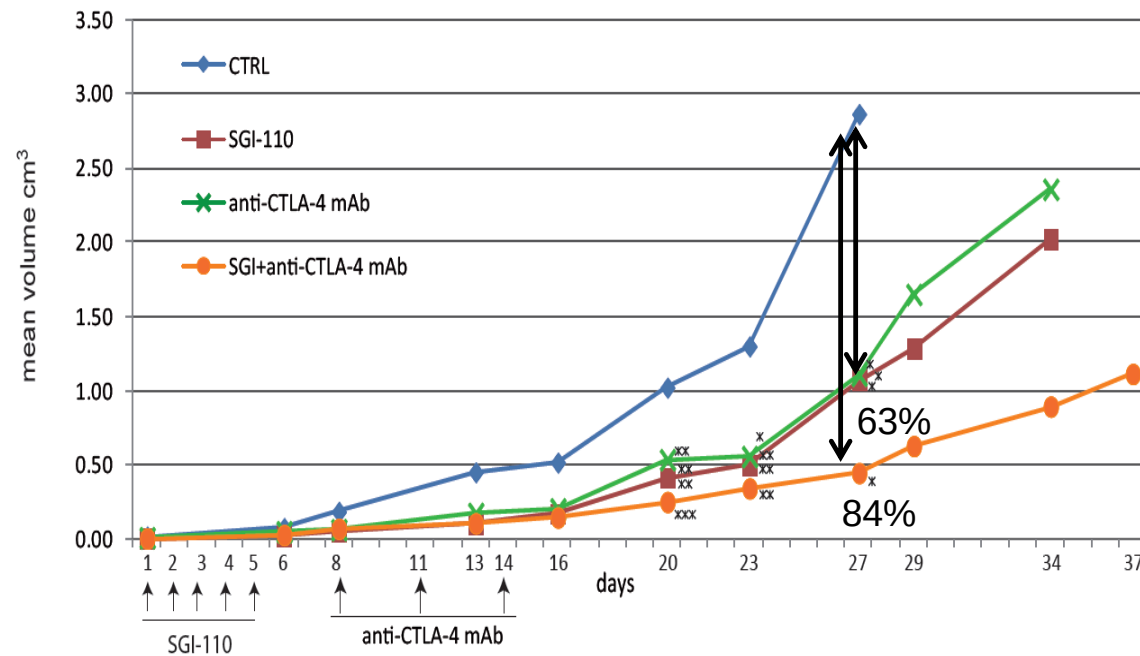


Immune desert tumors

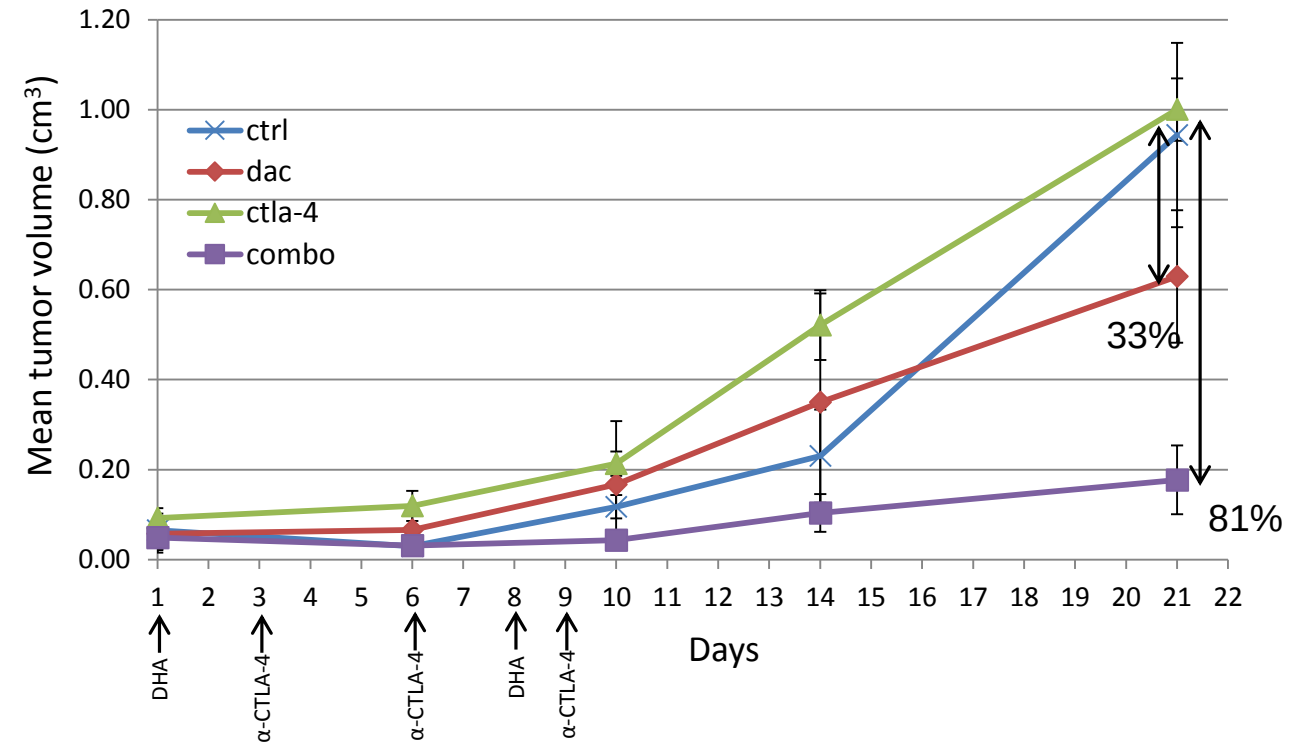




Anti-tumor activity of combo in different syngeneic mouse models



A. Covre et al., Semin Oncol 2015

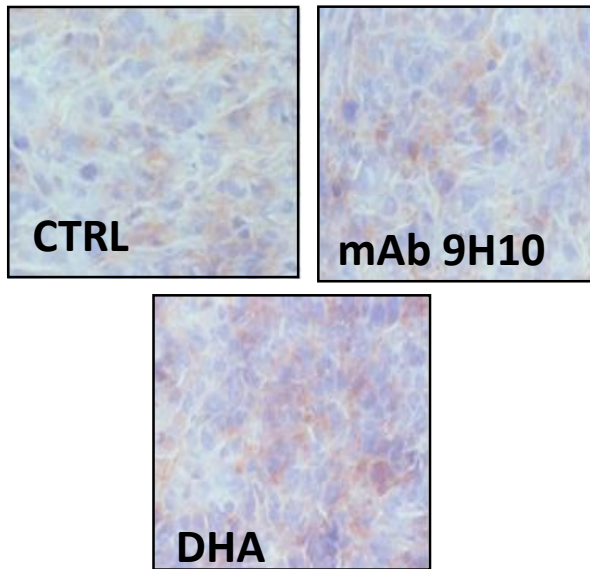


Covre A et al., OncoImmunology, 2015

IHC analysis of tumor and normal tissues

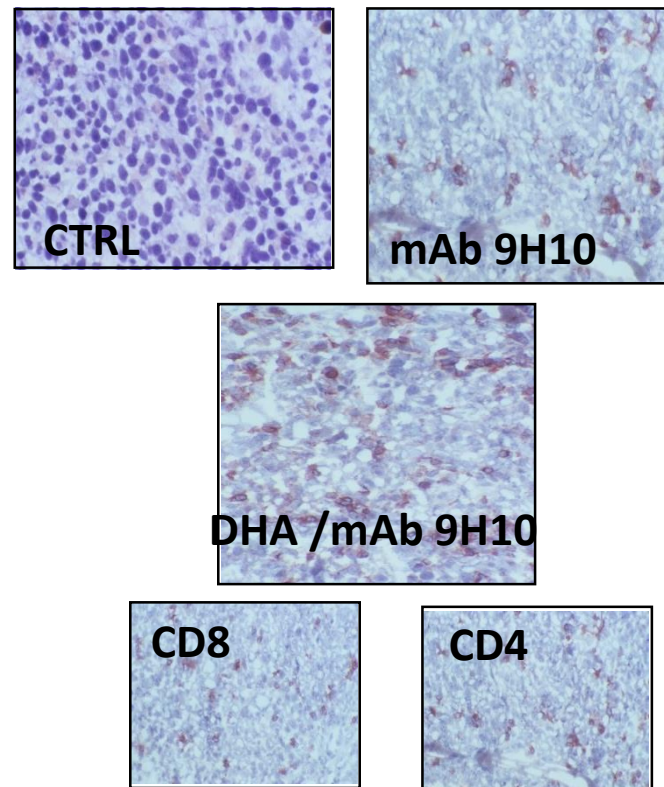
TUMOR

MHC class I



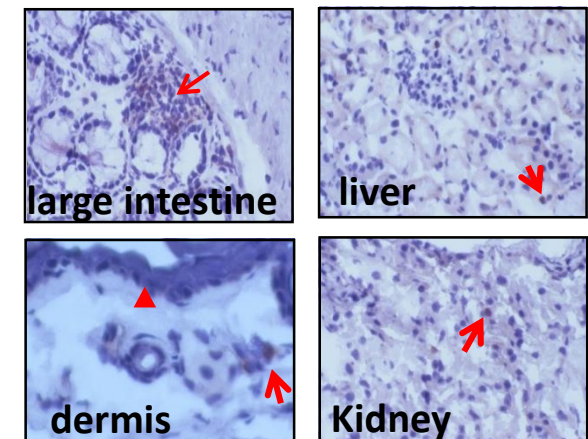
TUMOR

CD3

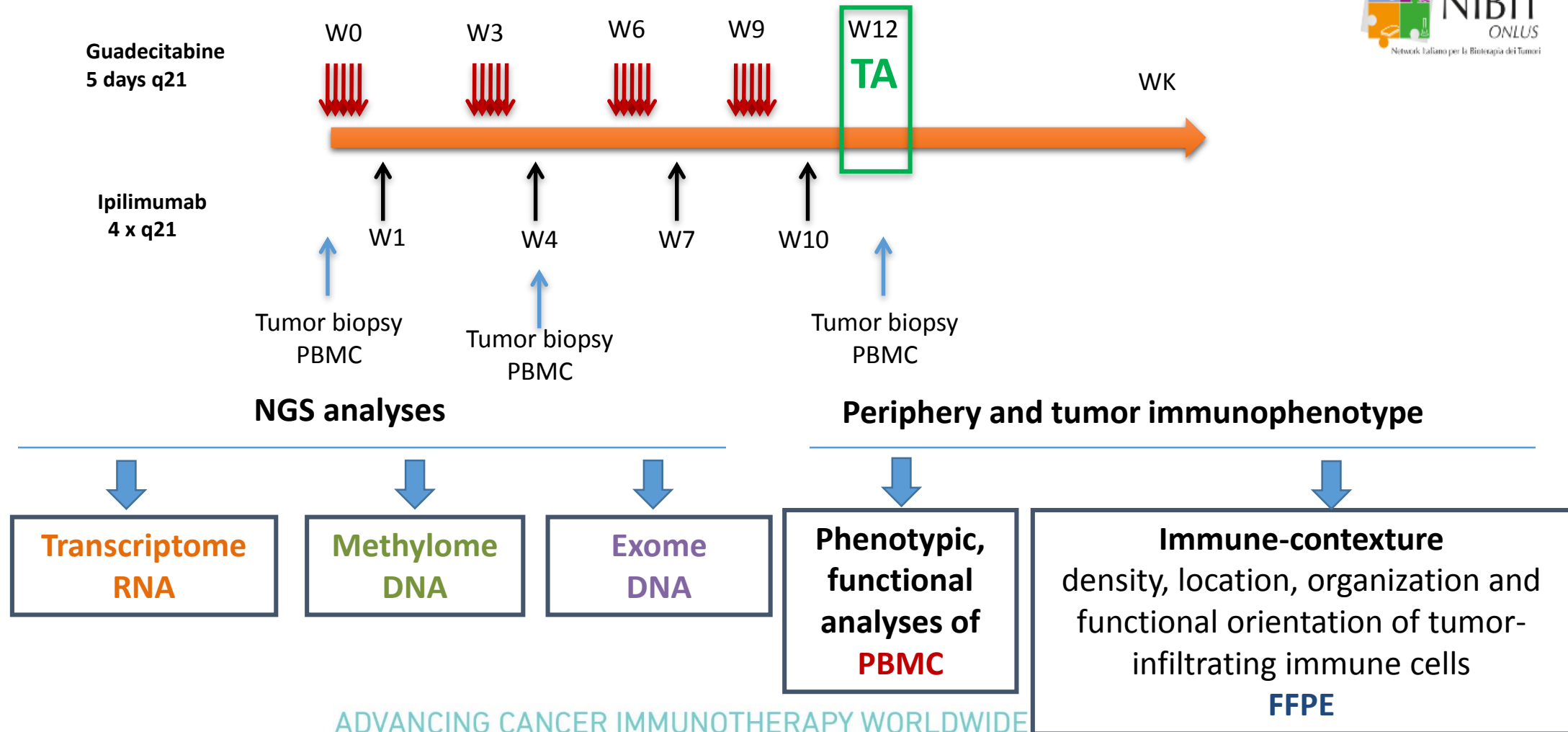


NORMAL TISSUES

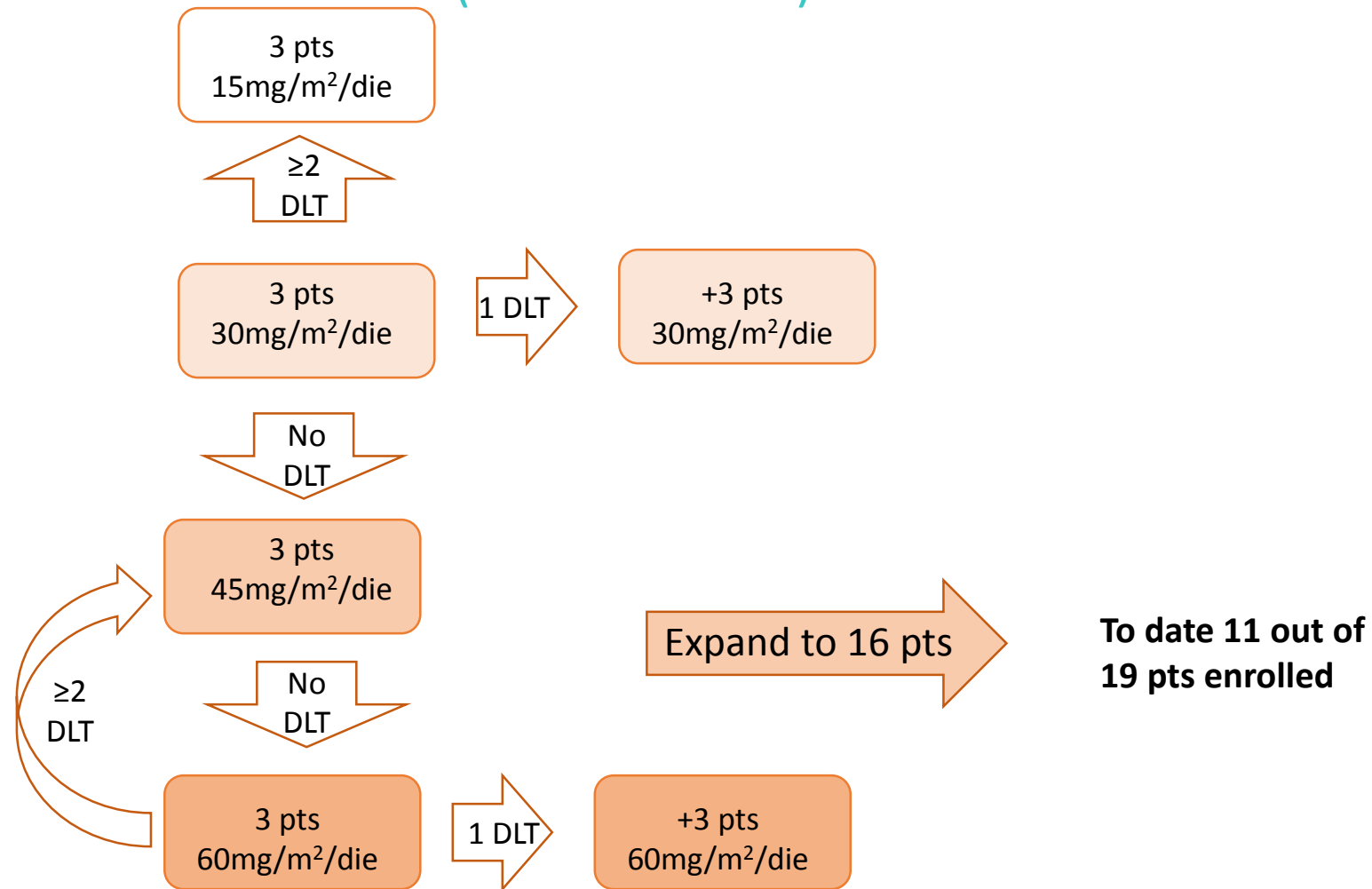
CD3



Epigenetic immuno-sequencing: the NIBIT-M4 Study (NCT02608437)



Epigenetic immuno-sequencing: the NIBIT-M4 Study (NCT02608437)





NIBIT FOUNDATION and CENTER FOR IMMUNO-ONCOLOGY UNIVERSITY HOSPITAL OF SIENA



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