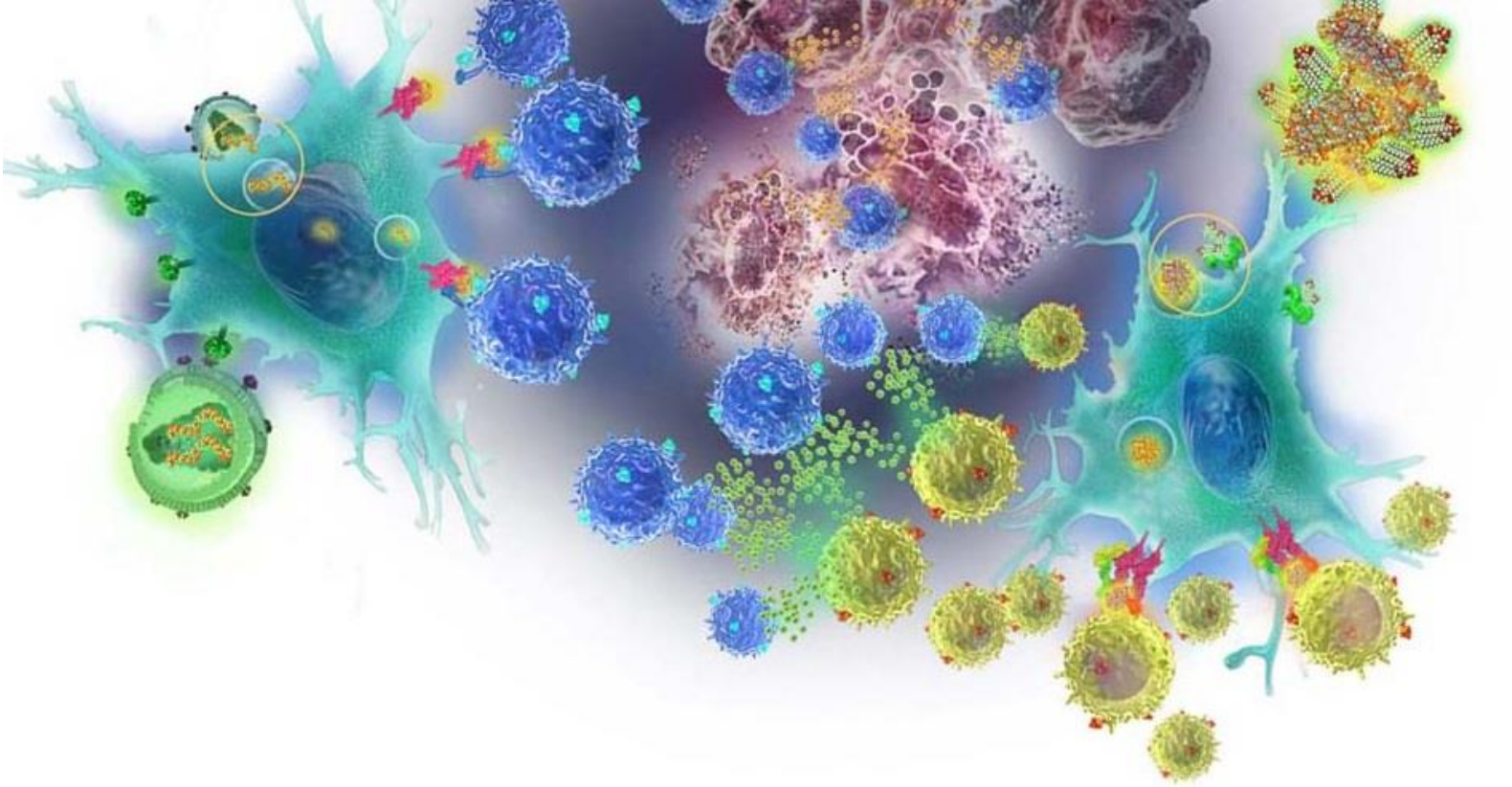


G100

POTENT INNATE IMMUNE ACTIVATOR

LECTURE: G100 + Pembrolizumab (Dr. Carlos Paya)
CONFERENCE: New Drugs in Hematology Conference (Oct 2018)

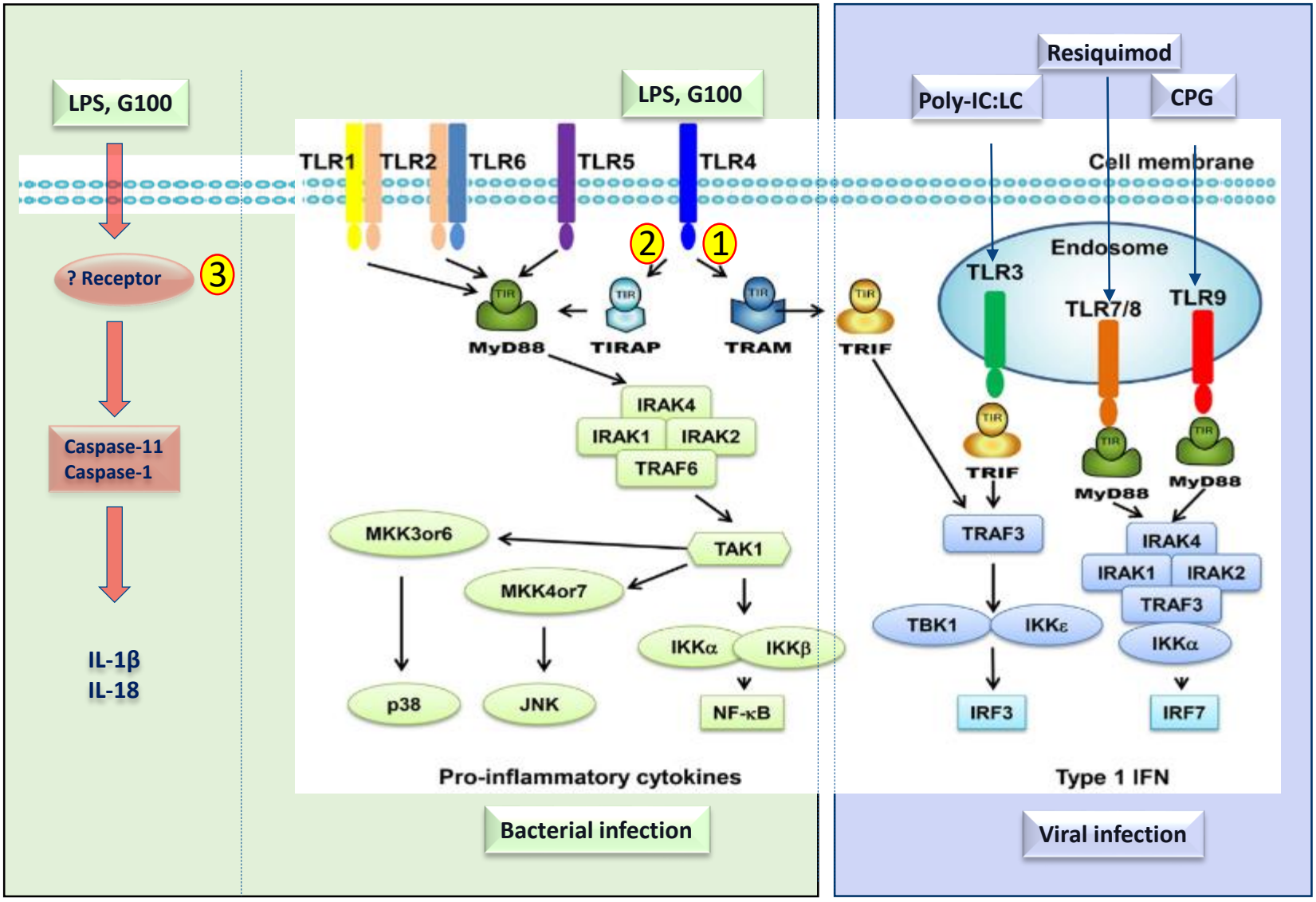
IMMUNE DESIGN

Forward-looking Statements

This presentation contains forward-looking statements with respect to, among other things, our business, financial condition, strategy and prospects, and has been prepared solely for informational purposes. All statements, other than statements of historical fact, regarding our strategy, potential future products, prospects, plans, opportunities and objectives constitute “forward-looking statements.” These statements are not guarantees of future performance and involve a number of unknown risks, assumptions, uncertainties and factors that are beyond our control. Given these risks, assumptions and uncertainties, you should not place undue reliance on these forward-looking statements.

Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, our history of net losses and expected net losses for the foreseeable future, that we have no product candidates approved for commercialization and may never achieve profitability, that we will require additional capital to finance our operations, that we may not be able to successfully develop, obtain regulatory approval and commercialize our product candidates, all of which are novel and in early clinical development, and those other risks that will be set forth under the header “Risk Factors,” “Note Regarding Forward-Looking Statements” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our periodic reports filed with the Securities and Exchange Commission, including our Quarterly Report for the period ended June 30, 2018. All statements contained in this presentation are made only as of the date of this presentation and are subject to uncertainty and changes. Except as required by law, we expressly disclaim any responsibility to update such forward-looking statements, whether as a result of new information, future events or otherwise.

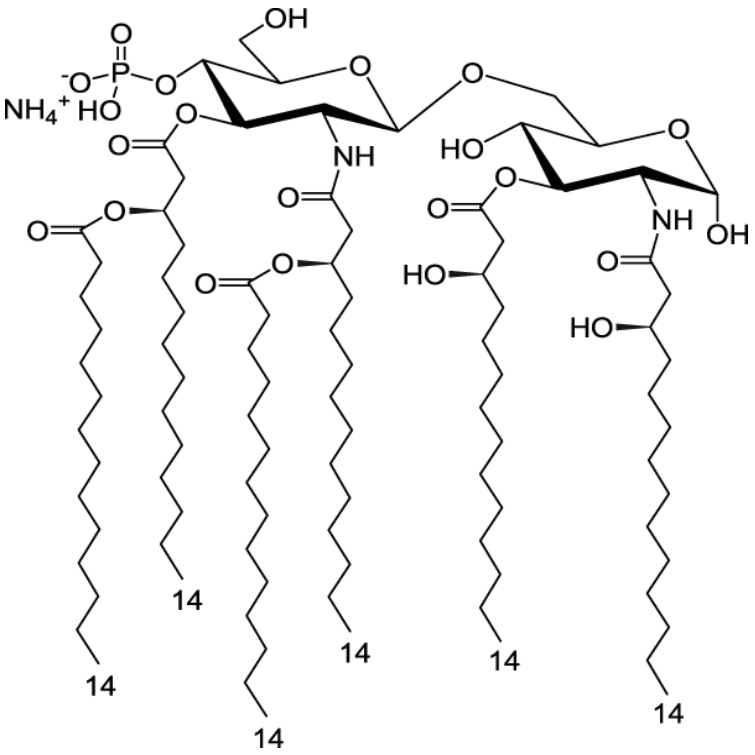
TLR4 Signaling: 3 Independent Pathways



Modified from: Zhao, Front Immunol 2013 and Desbien et al., Eur J Immunol. (2014)

IMMUNE DESIGN

Powerful + Safe Activator of TME Innate Immunity

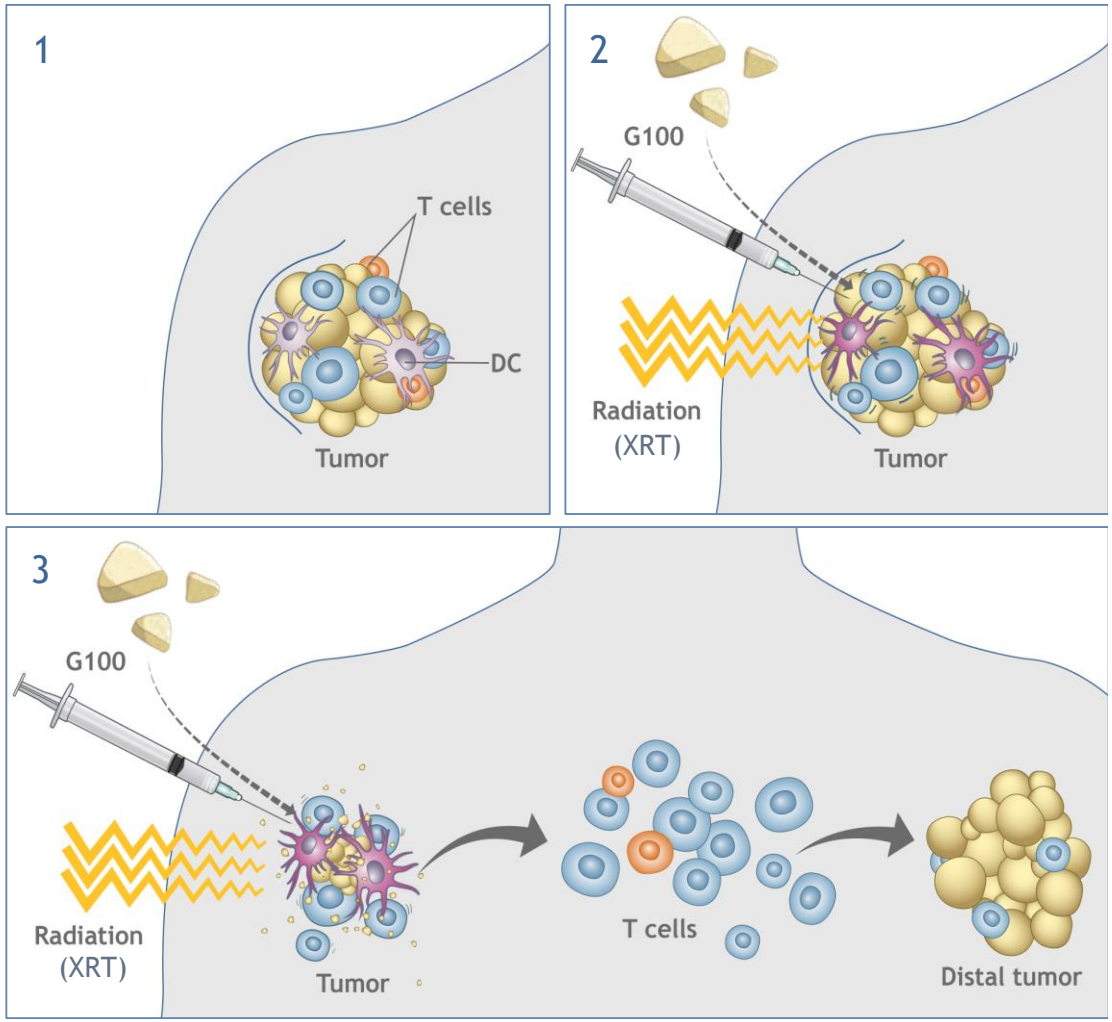


G100: GLA at the Core
(Glucopyranosyl lipid A)

- GLA is the first small molecule from IMDZ's *TLR4* agonist platform
- GLA is formulated for efficacy:
  - The squalene emulsion formulation (GLA-SE) provides a depo effect and allows for intracytoplasmic internalization; this compound is named ***G100***.
  - An aqueous formulation (GLA-AF) only binds the extracellular receptor
- API manufacturing uses chemical synthesis with strong IP
- >1000 pts exposed as a vaccine adjuvant and > 100 pts as an intratumoral agent with no Grade ≥3 SAEs

IMMUNE DESIGN

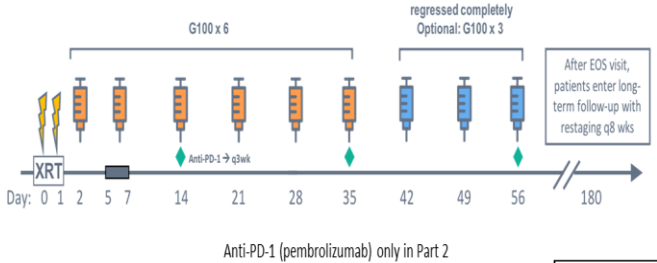
G100 Acts Locally to Drive Systemic Benefit



1. Targets TLR4 in any accessible tumor via
   - TME Dendritic cells leading to enhance antigen presentation and cytokine and chemokine production, and overall inflammation
   - Malignant B cells become exposed to incoming T and NK cells.
2. Attracts and expands pre-existing T and NK cells
3. Effective in combo w/ other agents (e.g. ACT, IMiDs, checkpoint inhibitors, others)
4. Designed for local tumor control + systemic immunity to control distant, non-treated tumors (abscopal effect)

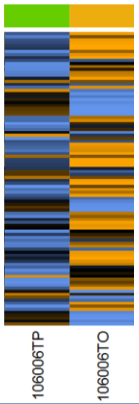
G100 Induces Proinflammatory Cytokine/Chemokine Milieu

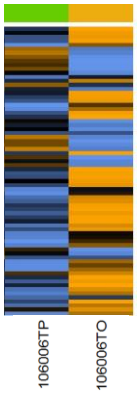
INCREASED CD8 TILS IN FL PATIENTS



106006TP: pre-G100 tumor biopsy
106006TO: post-G100 tumor biopsy

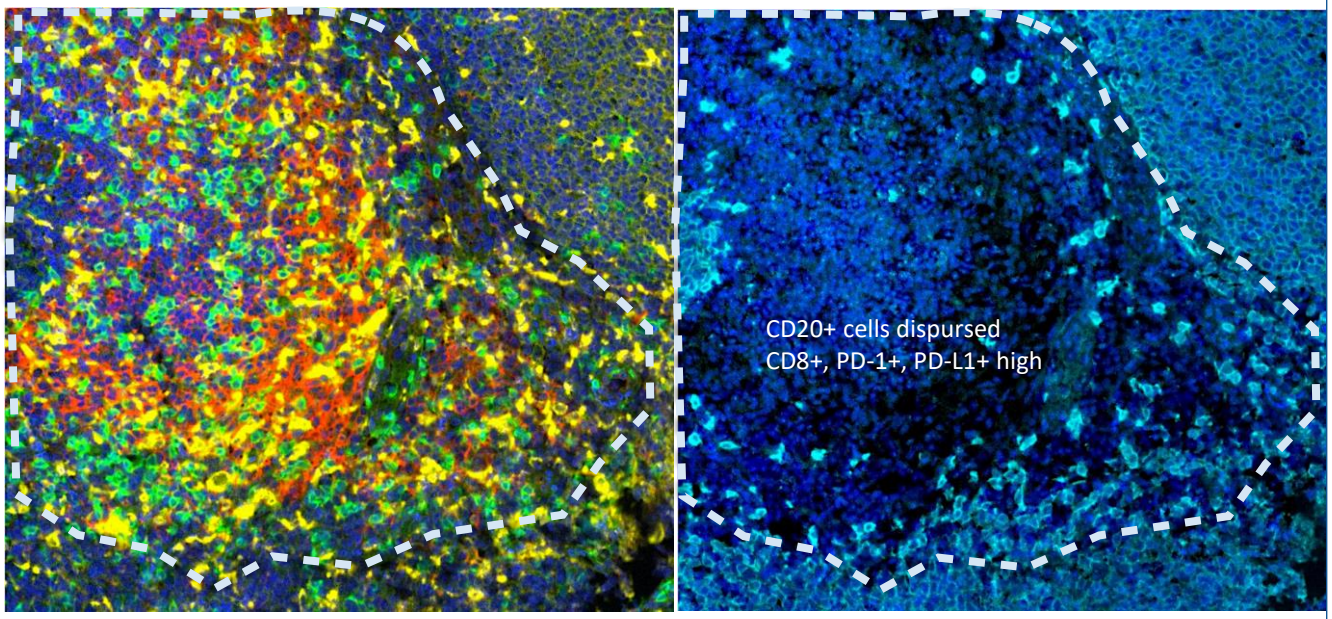
panCancer Immune Profiling





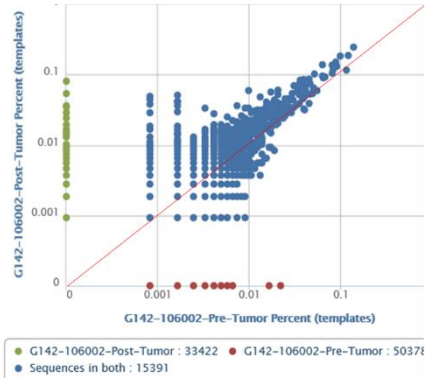
During G100 Treatment

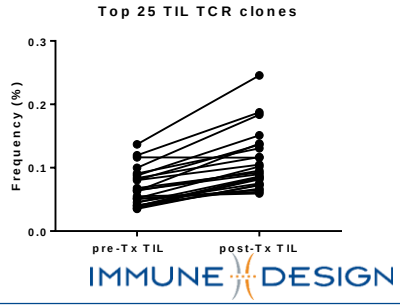
Infiltration of CD8 (Green) and macrophage (Yellow) co-localize with Disrupted Tumor Cells (CD20, Cyan Blue)



Green: CD8; Yellow: CD68; Cyan Blue: CD20; Red: PD-L1; Magenta: PD-1

TCR sequencing indicates clonal expansion of TILs in tumor post-G100





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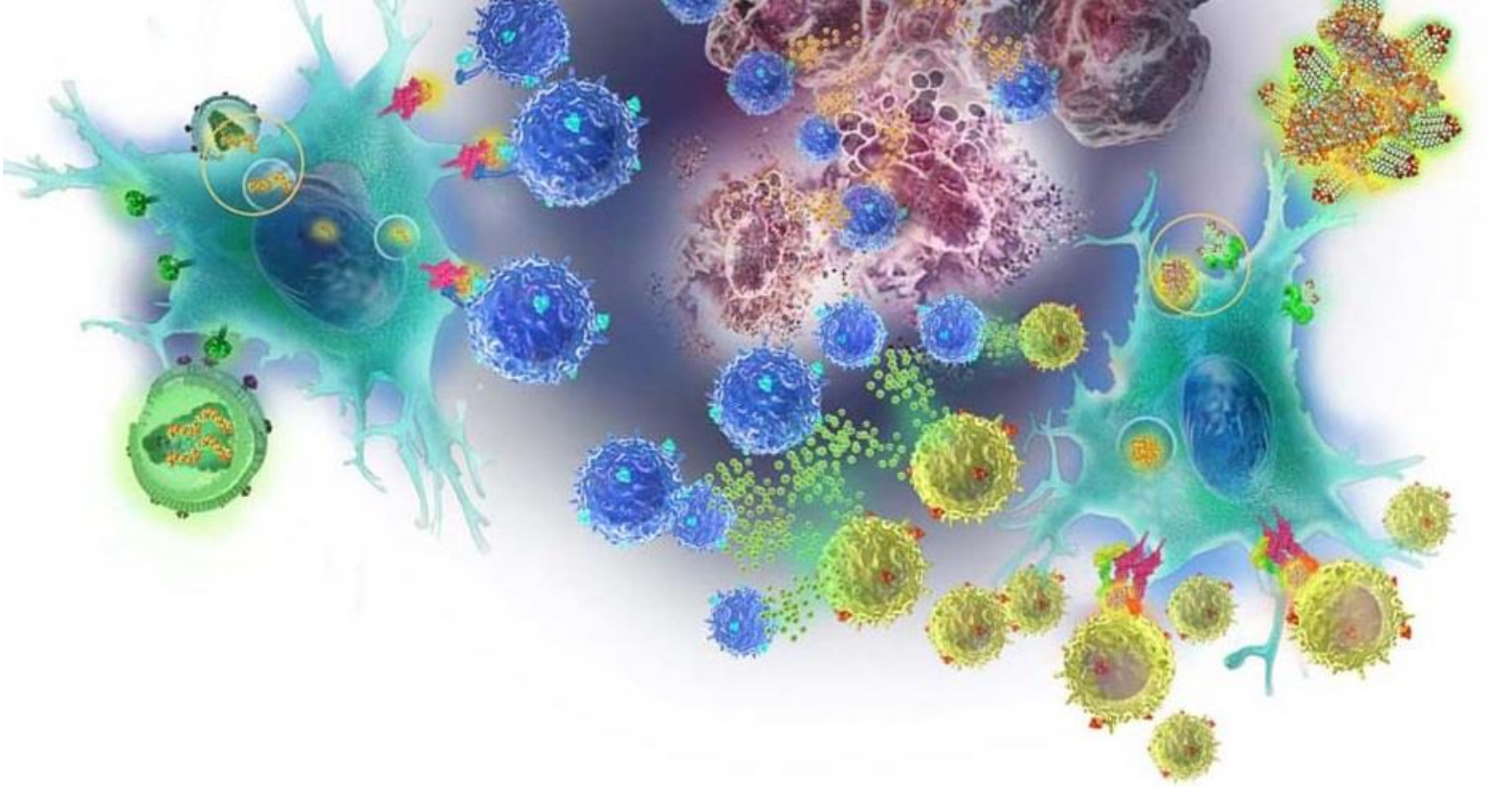


G100

DEVELOPMENT IN FOLLICULAR LYMPHOMA: FIRST PIVOTAL PATH

IMMUNE DESIGN

G100 Clinical Benefit in Follicular Lymphoma

INITIAL PATH IN UNMET NEED POPULATION

- Earlier trial design and goal: inject G100 into radiated lesion and observe distal, non-treated lesions to confirm systemic effect from local injection ***- achieved***
- Activity shown in relapsed/refractory & naïve patients: moving forward in patients with three prior therapies (unmet need[1]), with strategy to expand to earlier lines
- Potential to be the first chemotherapy-free, immunotherapy regimen in FL

Monotherapy

Ph 1 Dose Escalation
G100 5, 10, 20ug + XRT (n=9)

ASCO 2017

20ug Dose Expansion
G100 20ug + XRT (n=14)

Targeting Fall Medical Congress[2]

Combination Therapy

Ph 2 Randomized (10ug)
G100 + XRT (n=13)
G100 + XRT + pembrolizumab (n=13)

ASH 2017 & Q1'18 Update

Upcoming Pivotal Ph 2
G100 + Pembrolizumab[3]

- **FDA concurs on single-arm trial with ORR/DOR endpoints**
- **Adaptive design will refine final study; intended to support a BLA[4]**

[1]Per interactions with FDA [2]Presentations subject to acceptance. [3]Regimen not finalized – under discussion with FDA. [4]Dependent on study design agreement with FDA, as well as data

G100 +/- Pembrolizumab Phase 2

PATIENT CHARACTERISTICS

		G100 (n=13)	G100 + P (n=13)
Age: median (range)		**64 (39-72)**	**58 (36-80)**
Gender, M/F		**10M/3F**	**10M/3F**
ECOG, 0 / 1		**10 / 3**	**11 / 2**
Grade	1 / 2 3 Unknown/Missing	**11 (85%)** **2 (15%)**	**10 (77%)** **2 (15%)** **1 (8%)**
Stage At Entry	IIA/B IIIA/B IVA/B Unknown/Missing	**1** **6** **5** **1**	**0** **8** **5** **0**
Prior Treatment	Naïve R / R	**6 (46%)** **7 (54%)**	**8 (62%)** **5 (38%)**
	#Tx: 1-2 $\geq$3 Median (Range)	**2 (15%)** **5 (39%)** **3 (1 to 5)**	**2 (15%)** **3 (23%)** **4 (1 to 6)**
	Prior Auto-SCT	**3**	**2**
Growing Tumor at Entry		**6 (46%)**	**8 (62%)**

G100 +/- Pembrolizumab Phase 2
SAFETY

- Overall, the majority of AEs reported were Grade 1 or 2 for both treatment arms and the number of events were similar in both treatment groups

Patients with at least 1 TEAE	G100 (n=13)	G100 + P (n=13)
All	9 (69%)	11 (85%)
Grade 1	6 (46%)	6 (46%)
Grade 2	3 (23%)	4 (31%)
Grade 3	0	1 (8%)[1]
Grade 4	0	0
Grade 5	0	0
SAE	0	1 (8%)[1]

[1]There was 1 SAE and grade 3 event that occurred in a single patient on the G100+P arm which was considered related to pembrolizumab and not G100

G100 +/- Pembrolizumab Phase 2

EFFICACY

- Combination w/ pembro is synergistic (pembro monotherapy 11% ORR; similar to other αPD-1s)[1]
- Data initially presented at ASH 2017, updated in March 2018

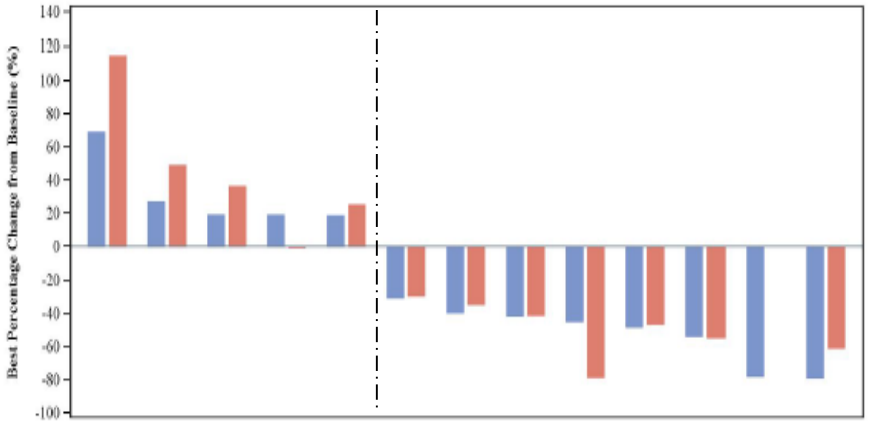
	G100 (n=13)	G100 + P (n=13)
Best Objective Response Rate (all lesions)[2]		
ORR (PR, pts (%) (-50% to 100%)	2 (15%)	7 (54%)
Treatment naïve [PR, pts (%)]	0/6 (0%)	3/8 (38%)
Relapsed/Refractory [PR, pts (%)]	2/7 (29%)	4/5 (80%)
PD, pts (%)	2 (15%)	1 (8%)
Abscopal Tumor Reduction (Min 10% - non-injected distal lesions)		
Overall, pts (%)	7 (54%)	10 (77%)
Range of shrinkage, %	22% - 79%	10% - 89%
Shrinkage ≥10cm^2, pts (%)	3 (23%)	5 (39%)

[1]Pembrolizumab and cemiplimab showed 11% and 9% ORR, respectively, at ASH 2017; nivolumab showed 40% ORR in 10 patients, which the company views as a relative outlier. [2]Responses are best responses in all index lesions combined (injected and non injected) with or without follow-up confirmation based on irRC (Wolchok, et al., 2009). Data cut off: 28Feb2018

G100 +/- Pembrolizumab Phase 2

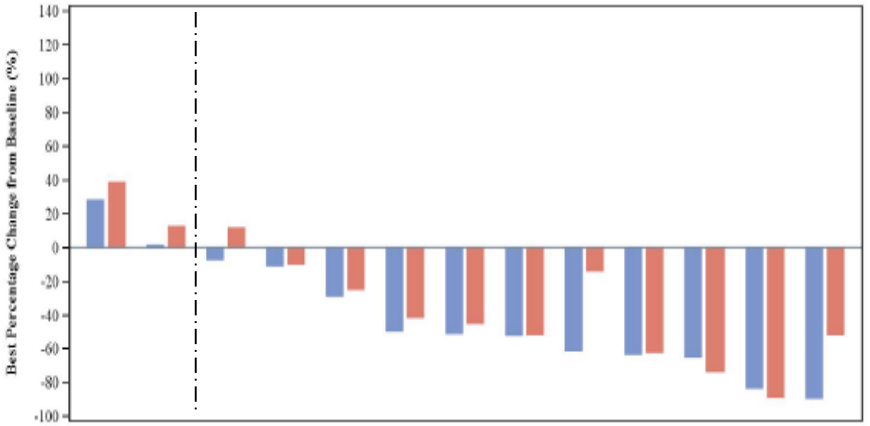
CONCORDANCE BETWEEN ALL AND ABSCOPAL LESIONS

G100 (n= 13)



All lesions	5	3	9	2	6	4	8	7	5	6	10	2	7
Abscopal lesions	4	1	8	1	5	3	7	6	4	5	9	0	6

G100 + P (n= 13)



All lesions	7	7	7	5	6	6	8	4	3	7	7	4	3
Abscopal lesions	6	6	5	4	5	5	6	3	2	6	5	1*	1

- Total Best % Change from Baseline of Sum of Product Diameters (SPD)
- Abscopal Best % Change from Baseline of SPD

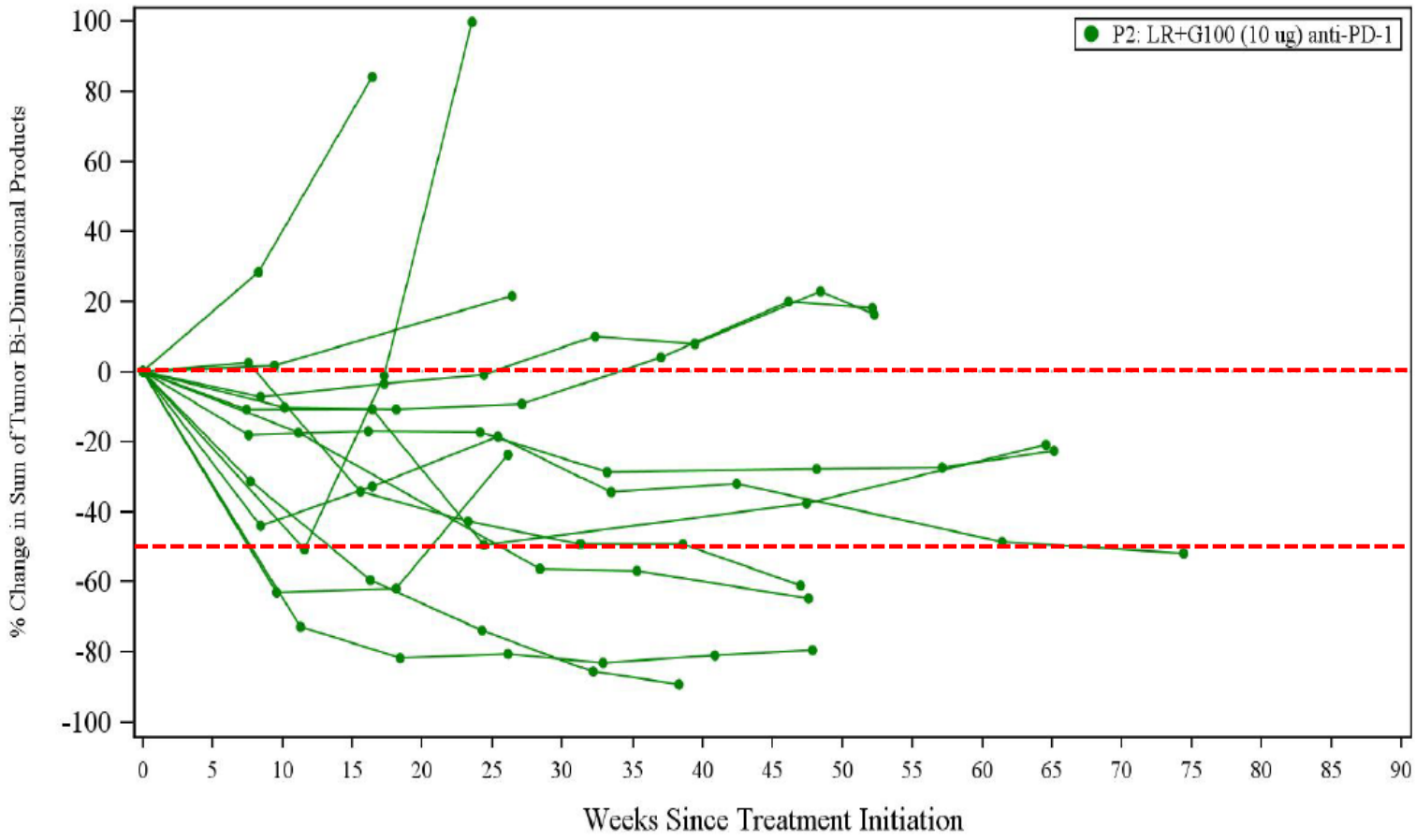
*Single baseline abscopal lesion was 4.5x3 cm

IMMUNE DESIGN

Ph2 G100 +/- Pembrolizumab

EFFICACY IN COMBINATION PATIENTS

- ORR progressive over time (n=13)



IMMUNE DESIGN

Ph2 G100 +/- Pembrolizumab

PROGRESSION FREE SURVIVAL (PFS)

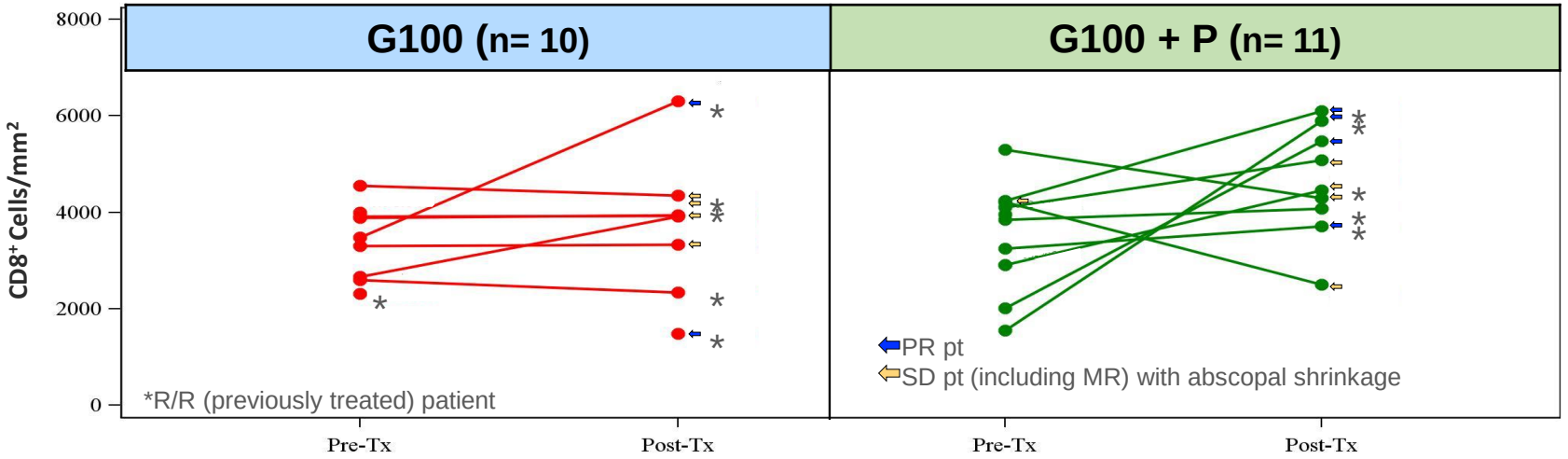
➔ Denotes patient has not progressed

Data cutoff Feb 28, 2018

IMMUNE DESIGN

Biomarker: Analysis of CD8+ TILs

- Addition of Pembro (P) demonstrated a trend to increased CD8+ TILs
- Association observed between increased TILs and clinical responses
- TIL increase appears to be dose dependent, evaluation of G at 20 µg ongoing; rationale for higher doses and combination with P



Immune Infiltrate	Responders	Non-Responders	Odds Ratio	p-value
CD8 (ratio of post/pre)	1.61	0.9	30	0.032
CD8/CD4 (ratio of post/pre)	2.99	1.14	5.1	0.054
CD8/Foxp3 (ratio of post/pre)	3.16	0.88	34	0.06

IHC analysis of pre and post tumors from patients in the Phase 1 dose escalation and this randomized phase 2 (n=36)

Tumor TLR4^{HIGH}: Potential G100 Predictive Biomarker

COMBINED PH1 DOSE ESCALATION AND PH2 RANDOMIZED TRIAL PATIENTS

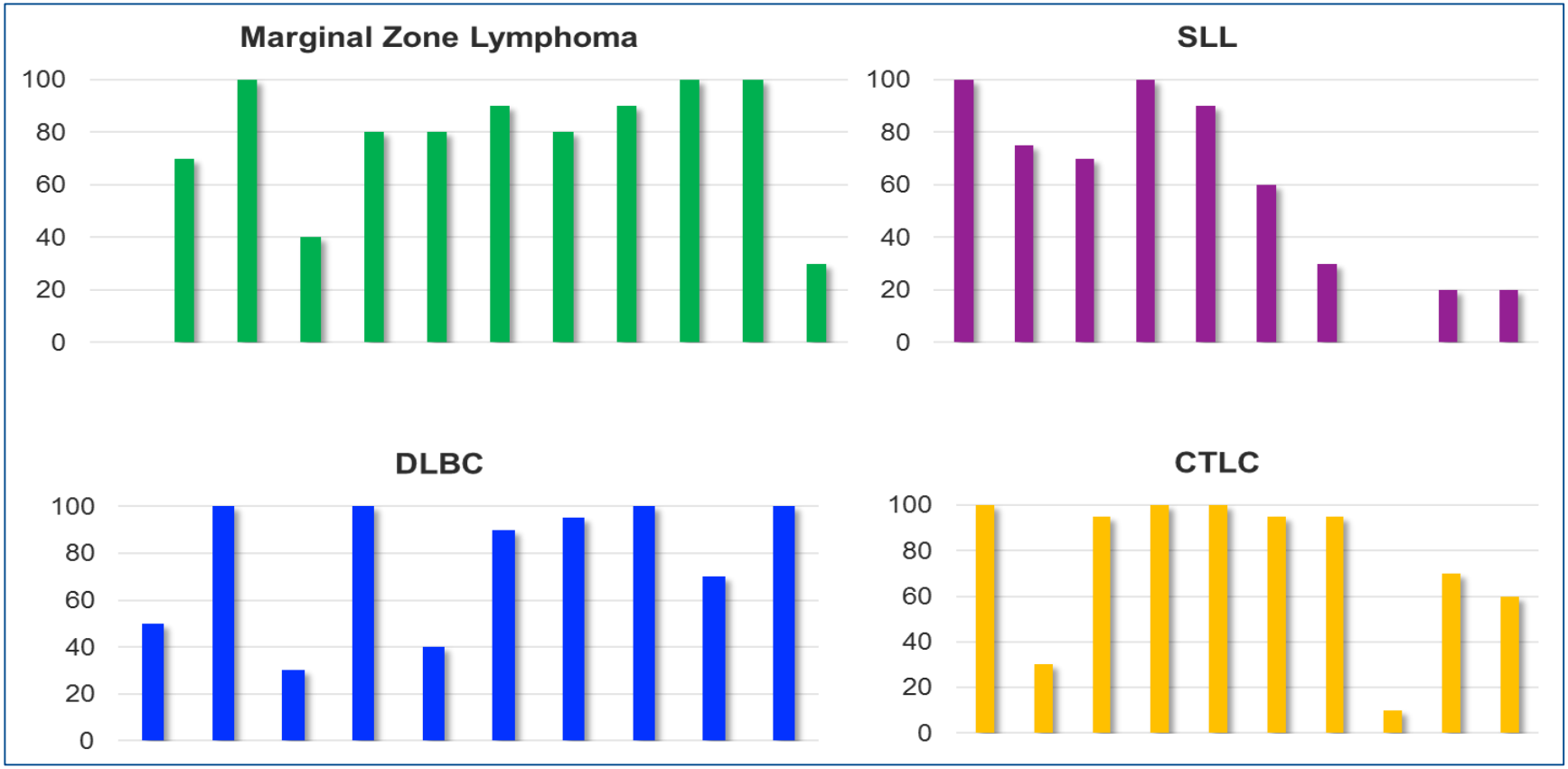
- Combined patients from Ph 1 (G100+XRT Dose Escalation) and Ph 2 (G100+XRT +/- Pembro) with available baseline biopsies were tested for tumor TLR4 expression and possible correlation with ORR

ORR for Combined Phase 1 Dose Escalation and Phase 2 Patients[1]		
	G100	G100 + P
Total pts treated	22	13
Pts with PRs (%)	5 (23%)	7 (54%)
ORR in TLR4^{HIGH} vs TLR4^{LOW} Patients[2]		
Total pts tested for baseline TLR4	18	12
TLR4^{HIGH} pts (%)	13/18 (72%)	8/12 (67%)
TLR4^{HIGH} pts with ORRs (%)	5/13 (38%)	6/8 (75%)
TLR4^{LOW} pts with ORRs (%)	0/5 (0%)	1/4 (25%)

TLR4^{HIGH} may provide a basis for patient selection and enrichment for responders in future development

[1]Responses are best responses in all index lesions combined (injected and non injected) with or without follow-up confirmation based on irRC (Wolchok, et al., 2009). [2]TLR^{HIGH} calculation is based on patients patients with ≥50% expression using IHC. Data cut off: 28Feb2018

TLR4 Expression is High in Other B Cell Malignancies



Tissue Biopsies from patients w/ different B cell malignancies were stained for TLR expression using IHC.

SLL: Small Lymphocytic Lymphoma; DLBC: Diffuse Large B cell lymphoma; CTCL: Cutaneous T cell lymphoma

Conclusions and Next Steps

- **G100 is a safe and potent TLR4 agonist that transforms a "cold" TME to a "hot" one**
  - Increased CD8 T cell infiltration with upregulation of PD1 and PDL1
  - Induction of chemokines and immune modulatory cytokines with decreased suppressive M2 macrophages
  - Activation of immature DCs with increased antigen presentation function
- **G100 (10ug) is safe (no grade 3 SAEs) and causes a systemic clinical response in both naïve and relapsed/refractory FL patients, which is further enhanced in combination with Pembrolizumab, achieving ORR's >50% w/ good durability**
- **The safety and efficacy of G100 at 20ug is being evaluated and its combination with Pembrolizumab is being planned in relapsed/refractory FL pts**
- **Biomarkers of efficacy (TIL induction and TLR4 expression in malignant B cells) may facilitate its development not only in FL but other B cell malignancies**
- **G100 could be the first active immunotherapy agent with single agent activity in lymphoma that is ideally suited to be combined with other non immunotherapy approaches (CD20's, PI3K's, bi-specifics, other) and CARTs**