MAYO CLINIC

Interactive Visual Exploration of Pairwise Meta-Analysis Results Huan He^{*}, Irbaz Bin Riaz ^{2,4,*}, Syed Arsalan Ahmed Naqvi², Rabbia Siddiqi³, Noureen Asghar³, Mahnoor Islam³, M. Hassan Murad⁴, and Hongfang Liu[†]

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Introduction

Cancer is a significant health problem, and its treatment can lead to physical and psychological issues which affect a patient's quality of life directly. A comprehensive summary of the treatment plan's benefit and harm outcomes will not only help researchers improve drug development, but also help clinicians make clinical decisions.

To summarize the findings and synthesize evidence for important clinical questions, pairwise metaanalyses (PMAs) are used to get precise estimates of treatment effects. However, it's challenging to explore the PMA results as complexity of clinical questions increase involving a huge number of studies and outcomes.

To address these limitations, we propose a visual analytics system to facilitate the PMA result exploration. Using this system, clinicians and patients can visualize the relevant data for shared decision making.

Task Analysis

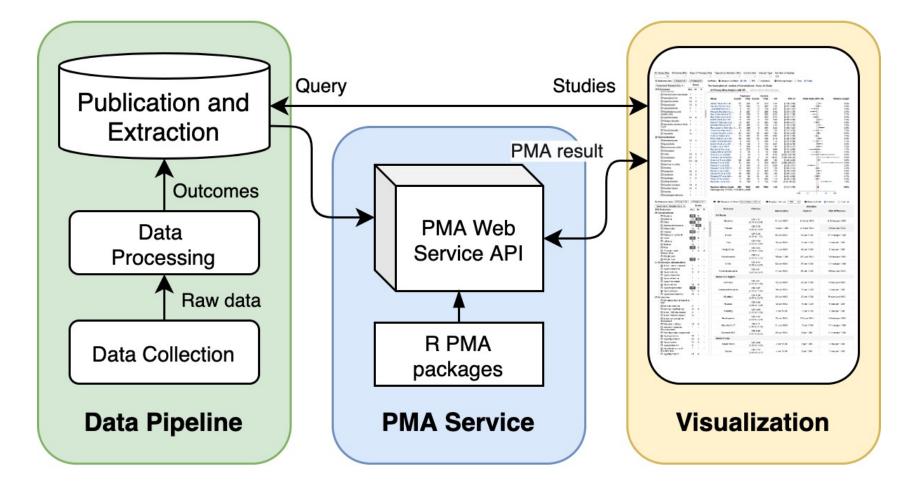
Due to the complexity of the PMA needs from the clinical question, we built a prototype system to validate the concepts and collect feedbacks based on an ongoing PMA project. The following domain goals are identified as the initial step to start our visual design and development:

T.1 How to best present safety and toxicity results for a given outcome from a particular drug? **T.2** How to best summarize the evidence across a range of outcomes to assess its overall performance?

Then, we identified the following design requirements:

R.1 Interactive exploration. **R.2** Exploration of different settings.

As shown in the following figure, our proposed system consists of three major modules: the data pipeline, the PMA service, and the visualization frontend.



T Filters | CI Class IIA O O PD1 O PD-L O CTLA ICI Name All Cancer Type Type of Therap 🔘 Ali O Com Mon Type of combi All Control Arm Clinical Settin All **Trial Phase** O Phase O Phas Type of Study

Primary Endp All Included in M O Yes O No

O Origin

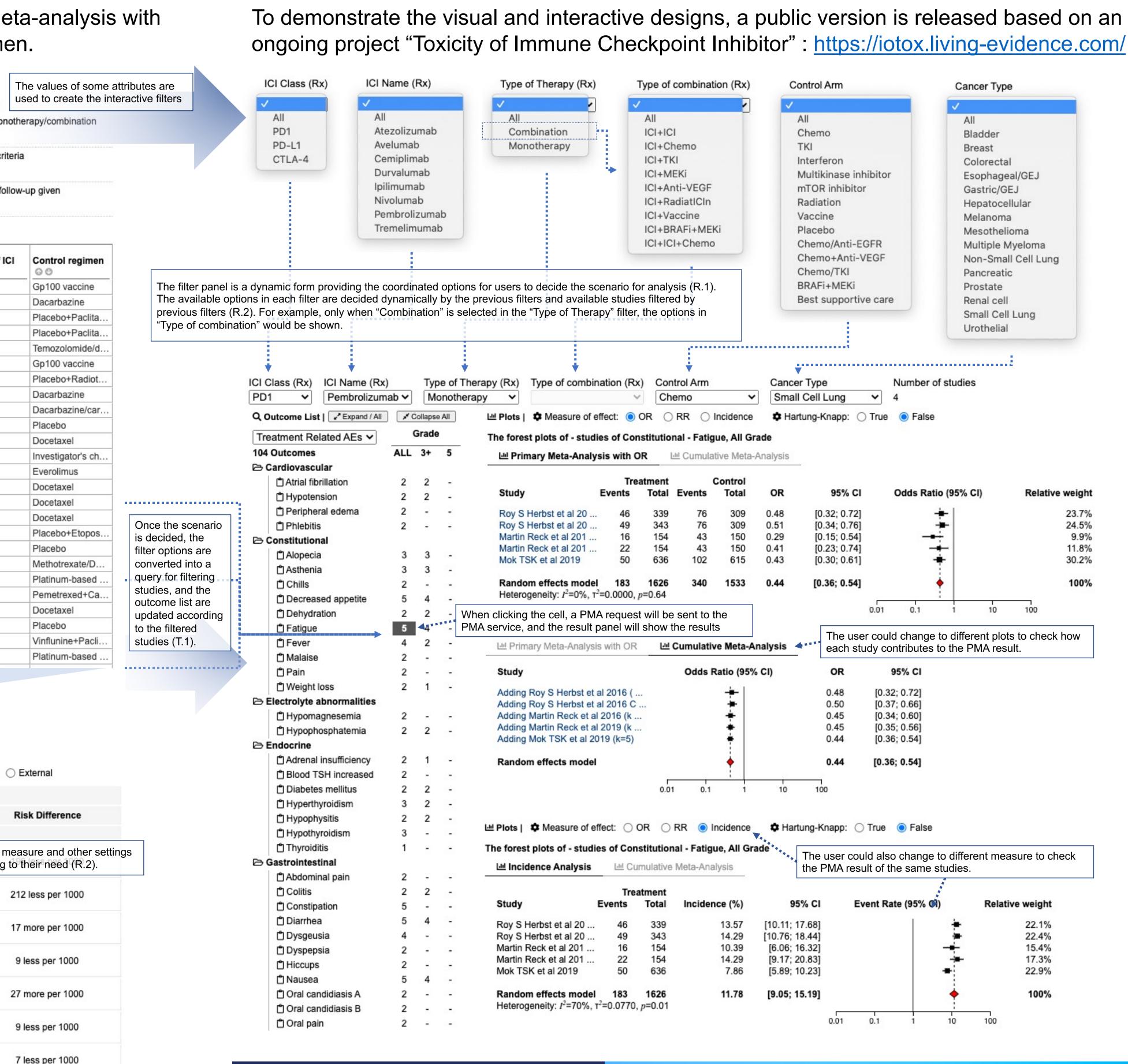
Interactivity Designs for Visual Exploration of Pairwise Meta-Analysis Results

The system provides an interactive table to show all studies included in the meta-analysis with detailed attributes, such as cancer type, treatment regimen, and control regimen.

2 Reset		🗖 Columns	Check All	O Reset All												
Θ		TRIAL VCT PMID Authors Year Original/Follow Up Study name VTrial phase Number of arms														
		CHARACTERISTICS														
				Type of combination				-		0						
L1								elation to ourgany	lo DD I 1 positivity i	inclusion crit						
A-4		POPULATION	POPULATION Total sample size Lines of treatment Clincal setting in relation to surgery Is PD-L1 positivity inclusion crit													
	~															
	0	RESULTS		Primary endpoint	Priamr	y Multiple, cor	mposite, or co-prima	ry endpoints? Sec	condary endpoint	Type of fol						
	*			Follow-up duration fo	or prima	ry endpoint(s)	in months [] Over	rall 🗌 Rx 🗌 Contro	1]							
	0	Data of Stud	iee 131 Re	cords												
	~					1										
ару	0	NCT	PMID © ©	Authors	Year	Trial phase	Cancer type	Treatment regimen	Name of ICI	Class of IC						
		NCT00094653	20525992	F Stephen Hodi	2010	Phase 3	Melanoma	Ipilimumab	Ipilimumab	CTLA-4						
nbination		NCT00324155	21639810	Caroline Robert	2011	Phase 3	Melanoma	Ipilimumab+Daca	Ipilimumab	CTLA-4						
otherapy		NCT00527735	22547592	Thomas J Lynch	2012	Phase 2	Non-Small Cell	Concurrent ipilim	Ipilimumab	CTLA-4						
bination (Treatment Arm)	0	NCT00527735	22858559	M Reck et al	2013	Phase 2	Small Cell Lung	Concurrent ipilim	Ipilimumab	CTLA-4						
	~	NCT00257205	23295794	Antoni Ribas et al	2013	Phase 3	Melanoma	Tremelimumab	Tremelimumab	CTLA-4						
	0	NCT00094653	23942774	McDermott D et al	2013	Phase 3	Melanoma	Ipilimumab	Ipilimumab	CTLA-4						
	~	NCT00861614	24831977	Eugene D Kwon	2014	Phase 3	Prostate	Ipilimumab	Ipilimumab	CTLA-4						
		NCT01721772	25399552	Caroline Robert	2015	Phase 3	Melanoma	Nivolumab	Nivolumab	PD1						
ng	0	NCT01721746	25795410	Jeffrey S Weber	2015	Phase 3	Melanoma	Nivolumab	Nivolumab	PD1						
	~	NCT00636168	25840693	Alexander M M	2015	Phase 3	Melanoma	Ipilimumab	Ipilimumab	CTLA-4						
	0	NCT01642004	26028407	Julie Brahmer et	2015	Phase 3	Non-Small Cell	Nivolumab	Nivolumab	PD1						
		NCT01704287	26115796	Antoni Ribas et al	2015	Phase 2	Melanoma	Pembrolizumab 2	Pembrolizumab	PD1						
se 2		NCT01668784	26406148	Robert J Motzer	2015	Phase 3	Renal cell	Nivolumab	Nivolumab	PD1						
se 3		NCT01673867	26412456	Hossein Borgha	2015	Phase 3	Non-Small Cell	Nivolumab	Nivolumab	PD1						
y .	0	NCT01905657	26712084	Roy S Herbst et al	2016	Phase 2	Non-Small Cell	Pembrolizumab	Pembrolizumab	PD1						
y .	0	NCT01903993	26970723	Louis Fehrenba	2016	Phase 2	Non-Small Cell	Atezolizumab	Atezolizumab	PD-L1						
		NCT01450761	27458307	Martin Reck et al	2016	Phase 3	Small Cell Lung	Ipilimumab+Etop	Ipilimumab	CTLA-4						
ow-up		NCT00636168	27717298	Alexander M M	2016	Phase 3	Melanoma	Ipilimumab	Ipilimumab	CTLA-4						
inal publication		NCT02105636	27718784	Robert L Ferris	2016	Phase 3	Head and Neck	Nivolumab	Nivolumab	PD1						
point	0	NCT02142738	27718847	Martin Reck et al	2016	Phase 3	Non-Small Cell	Pembrolizumab	Pembrolizumab	PD1						
	~	NCT02039674	27745820	Corey J Langer	2016	Phase 2	Non-Small Cell	Pembrolizumab+	Pembrolizumab	PD1						
/A	0	NCT02008227	27979383	Achim Rittmeye	2017	Phase 3	Non-Small Cell	Atezolizumab	Atezolizumab	PD-L1						
		NCT01057810		Tomasz M Beer	2017	Phase 3	Prostate	Ipilimumab	Ipilimumab	CTLA-4						
		NCT02256436	28212060	Joaquim Bellmu	2017	Phase 3	Bladder	Pembrolizumab	Pembrolizumab	PD1						
		NCT02041533	28636851	David P Carbon	2017	Phase 3	Non-Small Cell	Nivolumab	Nivolumab	PD1						

In addition to decide a specific scenario for analysis, the system provides an outcome comparison mode to support multi-outcome comparison in one view. All of the available studies in each outcome are used to create a summary of findings table to compare the overall performance (T.2).

Treatment Related AEs 🗸	Grad	e		_	×.	Absolute	
372 Outcomes	ALL 3+	5	Outcome	Relative	Intervention	Control	
➢ Constitutional		-	All Grade				
🗂 Alopecia	59 9	-	All Glade			The user can select dit	fforont m
🗂 Asthenia			Hypertension	OR 0.41 (0.22 to 0.73)	143 per 1000	to check the results according	
🗂 Chills	10 3	5					
Decreased appetite	93 24		Alopecia	OR 0.17	51 per 1000	244 per 1000	
Dehydration	14 6	2		(0.11 to 0.24)	19911111122000000000		
🗂 Fatigue	103 27	1	Chills	OR 1.44	E2 por 1000	27 par 1000	
Fatigue or asthenia	1 1		Chills	(0.72 to 2.87)	52 per 1000	37 per 1000	
🛱 Fever	30 6	1		OR 0.64			
Lethargy	6 1	-	Dehydration	(0.35 to 1.17)	16 per 1000	24 per 1000	
🗂 Malaise	12 1	-					
🗂 Pain	10 2	1	Fever	OR 1.39	86 per 1000	64 per 1000	
Physical health deterioration	4 2	2		(1.11 to 1.75)			
	4		Pain	OR 0.53	10 per 1000	19 per 1000	
C Weight gain	10 0		- cin	(0.32 to 0.88)		to per tooo	
Weight loss	19 9	<u>.</u>		OR 0.85		10 1000	
Electrolyte abnormalities	. 1		Weight loss	(0.51 to 1.44)	41 per 1000	48 per 1000	
	1 -	-		OR 8.24			
Hypercalcaemia	2 -	1	Adrenal insufficiency	(3.52 to 19.30)	0 per 1000	0 per 1000	
Hyperkalemia	92			(0.02 10 10.00)			
Hyperuricaemia	1 -	-	Grade 3 or higher				
Hypocalcaemia		<u></u>	Decreased expetite	OR 0.97	14 per 1000	15 per 1000	
Hypochloraemia	14 6		Decreased appetite	(0.59 to 1.58)	14 per 1000	15 per 1000	
🛱 Hypokalemia	14 6	2		OR 0.80			
Hypomagnesemia	17 4	-	Fatigue	(0.58 to 1.12)	22 per 1000	28 per 1000	
Hyponatremia	13 2	-		•			
Hypophosphatemia	11 4	<u>_</u>	Fever	OR 2.38	6 per 1000	3 per 1000	
Endocrine				(0.84 to 6.73)			
Abnormal thyroid function test	n 1 -	-	Hypokalemia	OR 0.48	14 per 1000	30 per 1000	
Adrenal disorder	2 -	2	Typontatornia	(0.16 to 1.43)	14 901 1000	00 por 1000	
Adrenal insufficiency	12 3		144.5.1.1	OR 2.33	0 4000		
Blood TSH decreased	5		Weight loss	(0.89 to 6.13)	6 per 1000	3 per 1000	
Blood TSH increased	13 -	-	Grade 5 only				
Blood corticotrophin	1 -	-	Grade 5 Only				
decreased			Sepsis	OR 0.72	2 per 1000	2 per 1000	
🗂 Diabetes mellitus	The user of	could sel	ect multiple outcomes and	(0.25 to 2.07)			
🗂 Diabetic metabolic			by grade into a table for	OR 0.41	0 (000	E 4000	
decompensati	compariso	on.	Pneumonia	(0.18 to 0.94)	2 per 1000	5 per 1000	



Future Work

Our domain experts appreciated the interactive designs and were able to effectively use the system to explore the PMA results. While the existing features provide enough details to see check the outcomes and assess the performance, limited support is available for figuring out the how are the changes when new studies are imported. In addition, the results should be further summarized for shared decision making in clinical practice.

Since our system is still in early stage, and there are still many MA results to be included in the system, we will work on improving the visual designs and developing the features for further use of the MA results in both clinical research and practice.

1 less per 1000

0 less per 1000

0 less per 1000

6 less per 1000

4 more per 1000

16 less per 1000

4 more per 1000

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