LiveHTA: Concept and Implementation Tools for the Future of Health Technology Assessments

Cytel ISPOR Theater

ISPOR Theater

Moderator

Bart Heeg, Vice President, Global HEOR, Cytel

Speaker 1

Grammati Sarri
Head of RWAA External Research Partnerships/ Senior Research Principal

Speaker 2

Anna Forsythe
Vice President, Value & Access

Speaker 3

Andre Verhoek
Research Principal

Cytel

HTA Current Reality

HTA staff and research limited capabilities

Healthcare system budget constraints

HTA challenges

Explosion of innovative, digital technologies and rise of precision medicine

Expanded use of RWE and HTA increased requirements for complex analytical methods

Drive for earlier patient access

Standard HTA Processes

- Submission of a dossier (clinical, economic, other evidence) by the manufacturer
- HTA body may commission an independent review.

- Review of evidence submitted by a panel
- Issues around acceptability, equity may be considered.

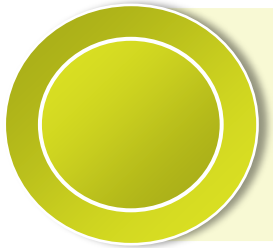
- Considering benefit of the technology
- Taking into account uncertainty in estimates and need for further data collection

Technology is recommended

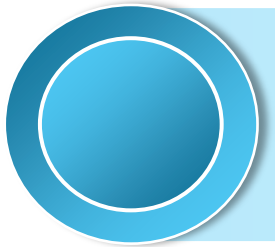
Technology is not recommended

Conditionally recommended

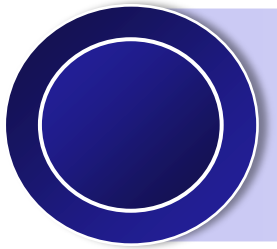
Challenges with Current HTA Processes



Health systems sustainability: de-reimbursed and economic threshold values

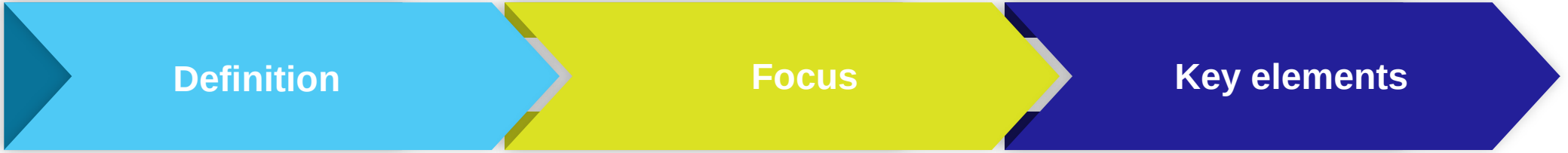


Evolving evidence and new methodological standards



Evidentiary uncertainty (patients, care pathway, technology, comparators)

LiveHTA as a Potential HTA Solution



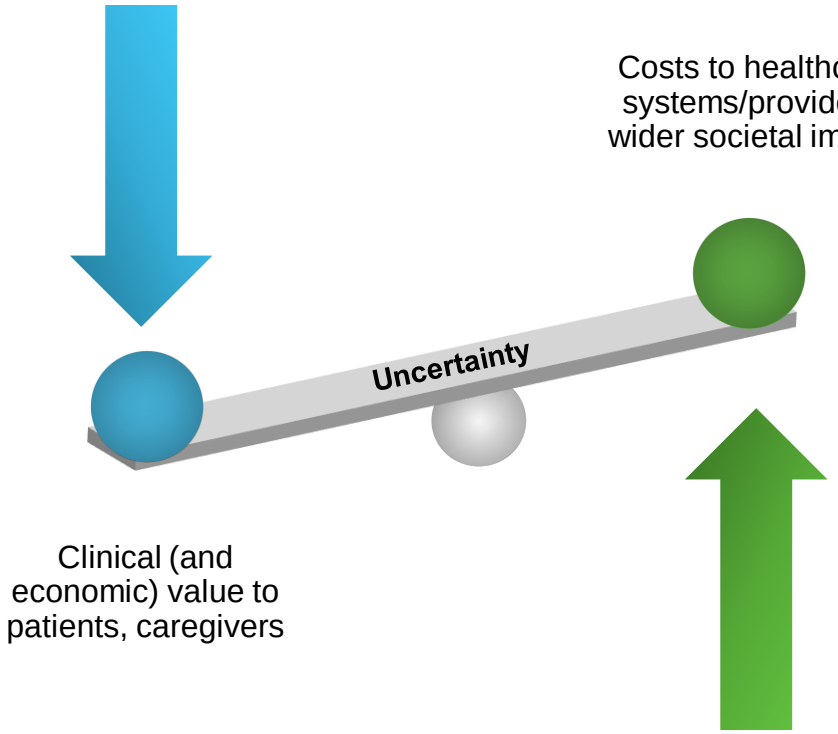
- Understanding of missed opportunities of single timepoint HTAs and the potential harm from lack of re-assessments for technologies (and the potential new comparators) in market for both patients and healthcare systems
- Lack of integration of technological advances in evidence synthesis and data analysis through automated tools and online applications

- An HTA process allowing the value of technologies to be re-assessed at different points in product's lifecycle
- Main aim is to respond rapidly to new evidence as it emerges, aiming to inform and update decision-making, if needed.

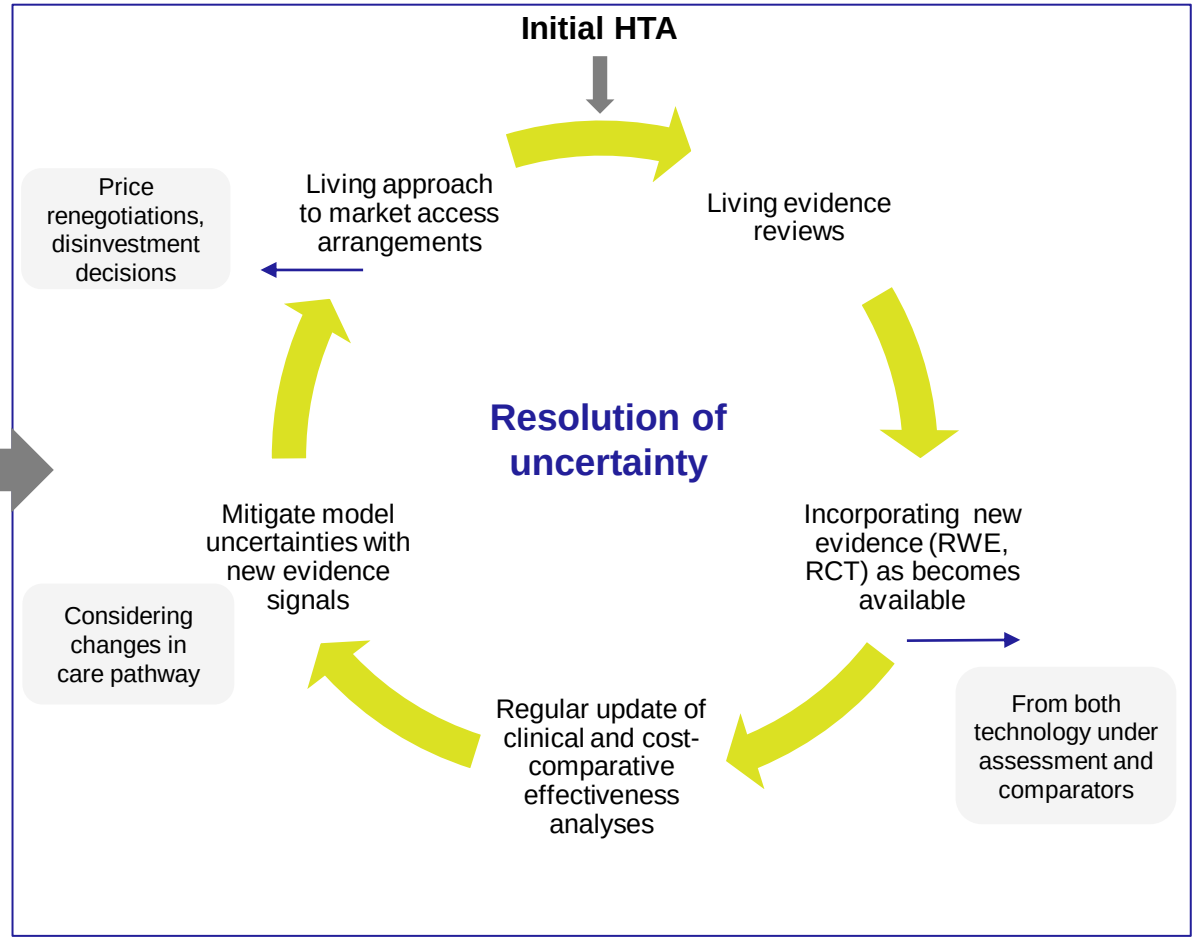
- Pre-determined commitment to **regular evidence updates** and assessments
- **Responsiveness** to evolving evidence
- **Standardized process** to transparently incorporate new evidence in decision-making
- Framework to allow trustworthy **integration of digital tools** in decision-making

Moving from a Static HTA To a Dynamic LiveHTA Process

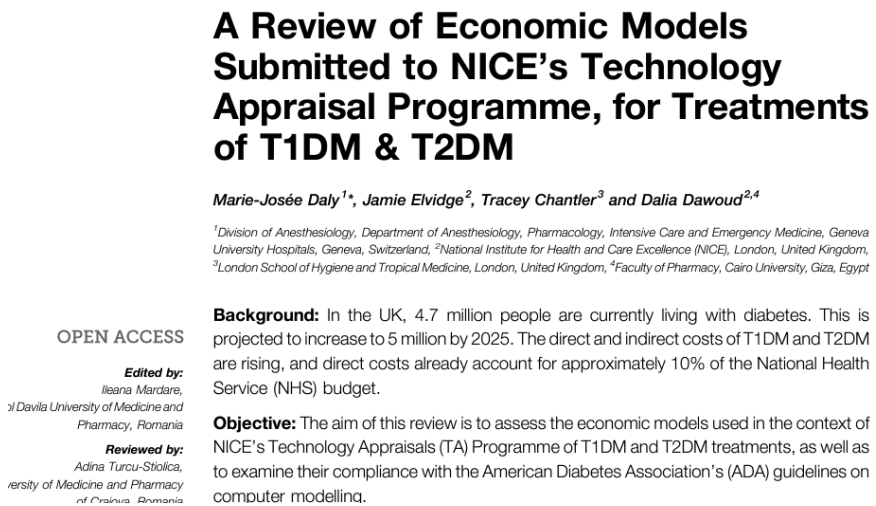
Static, single timepoint assessment



Dynamic, real-time LiveHTA process



Evidence for the Need of a “living” HTA Approach



A Review of Economic Models Submitted to NICE’s Technology Appraisal Programme, for Treatments of T1DM & T2DM

Marie-Josée Daly[1], Jamie Elvidge[2], Tracey Chantler[3] and Dalia Dawoud[2,4]*

[1]Division of Anesthesiology, Department of Anesthesiology, Pharmacology, Intensive Care and Emergency Medicine, Geneva University Hospitals, Geneva, Switzerland, [2]National Institute for Health and Care Excellence (NICE), London, United Kingdom, [3]London School of Hygiene and Tropical Medicine, London, United Kingdom, [4]Faculty of Pharmacy, Cairo University, Giza, Egypt

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Reviewed by:
Adina Turcu-Stiolica,
versity of Medicine and Pharmacy of Craiova, Romania

Background: In the UK, 4.7 million people are currently living with diabetes. This is projected to increase to 5 million by 2025. The direct and indirect costs of T1DM and T2DM are rising, and direct costs already account for approximately 10% of the National Health Service (NHS) budget.

Objective: The aim of this review is to assess the economic models used in the context of NICE’s Technology Appraisals (TA) Programme of T1DM and T2DM treatments, as well as to examine their compliance with the American Diabetes Association’s (ADA) guidelines on computer modelling.

Conclusions:

Diabetes medications and other technologies should also be subject to regular and consistent re-appraisal to inform disinvestment decisions. Artificial intelligence could potentially enhance models’ transparency and practicality.

Living Approaches to Healthcare Decision-making

- Living Guidelines Approach not NEW! (WHO, NICE, Australia)
- For HTAs, this is a new approach, although:
  - A life-cycle (LC)- HTA framework
  - During COVID-19, the best-practice guidance for the HTA of diagnostics and treatments for COVID-19 (HTx) noted different elements of "living approaches" to be incorporated in decision-making; from living systematic reviews to inform clinical effectiveness assessment to "living," adaptable whole-disease pathway economic models with regular updates to support a "living" HTA process.

HTx

Best-practice guidance for the health technology assessment of diagnostics and treatments for COVID-19

2.1.3. Evidence synthesis

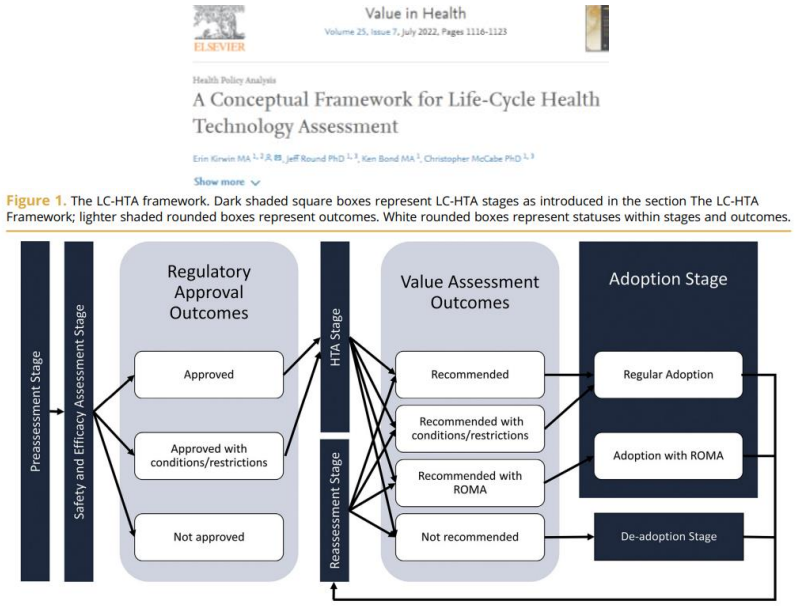
Recommendations

HTA agencies should consider the use of existing "living" clinical evidence reviews and meta-analyses to inform their clinical effectiveness decisions (29–31).

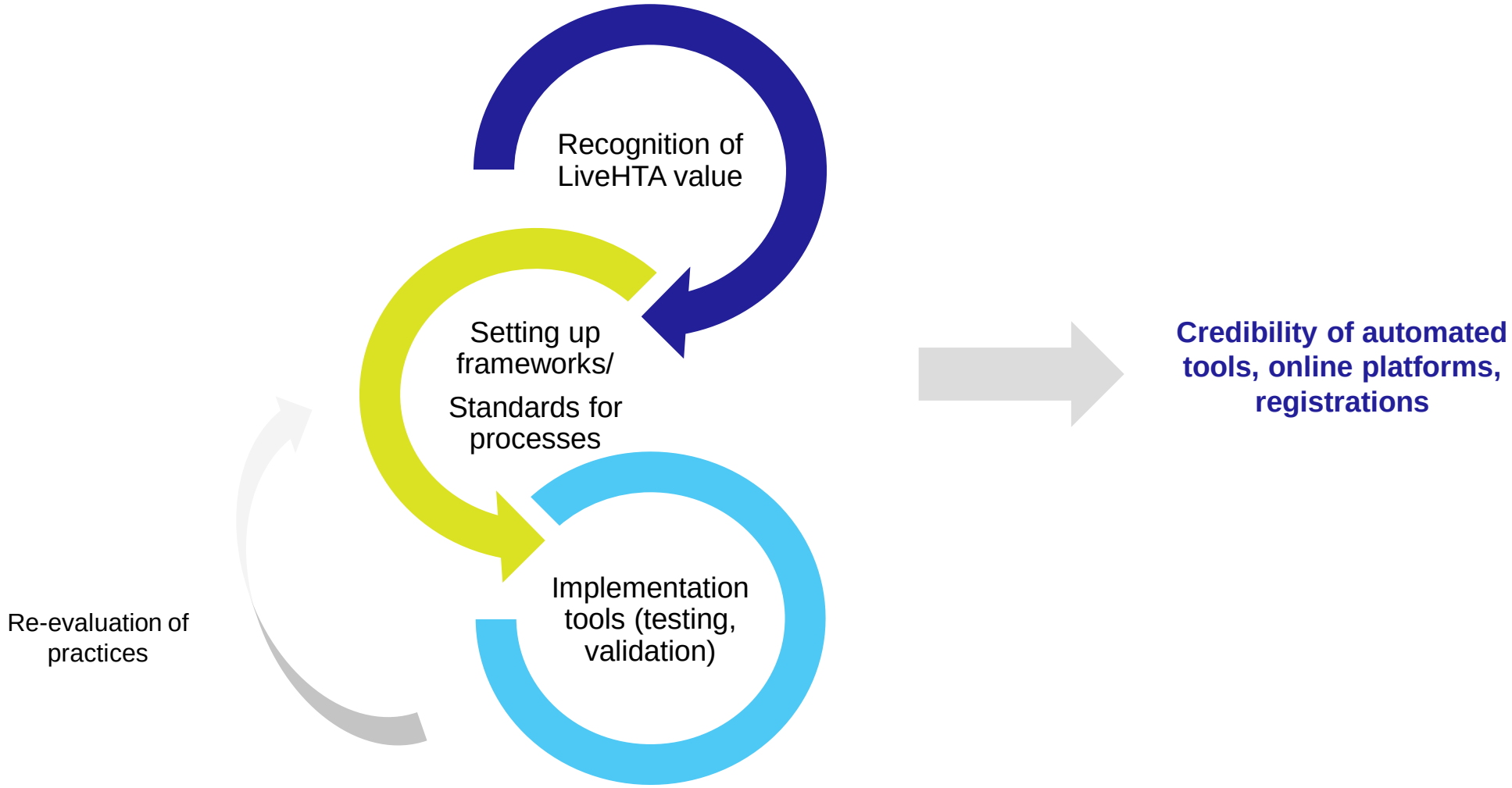
- While many agencies would prefer to conduct their own evidence reviews in normal times, the publicly available and frequently updated living reviews provide a pragmatic way of assessing the clinical effectiveness of treatments for COVID-19. Using these sources will reduce duplication of work and may allow for quicker assessments.

HTA agencies should carefully and transparently consider the generalisability of evidence from an external living review, consistent with the recommendations in section 2.1.1.

HTA agencies should consider developing a generic "living" disease model for the diagnosis and treatment of COVID-19 that can be adapted to different jurisdictions (see section 4.6).



What Is Next?


Recognition of LiveHTA value
Setting up frameworks/
Standards for processes
Implementation tools (testing, validation)
Re-evaluation of practices
Credibility of automated tools, online platforms, registrations

Future of HTA

For HTA purposes, we are developing typically standalone documents.

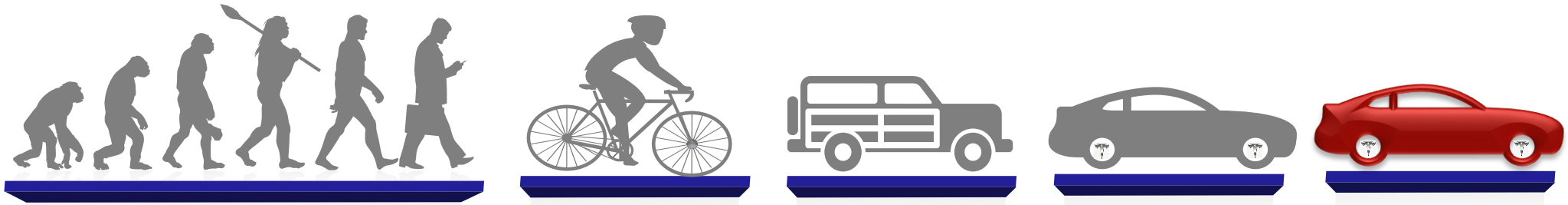
- Systematic literature reviews
- Network meta-analyses
- Cost-effectiveness analyses
- Budget impact analyses
- Global value dossiers
- Local HTA submission dossiers

Over time, these need to be updated because new pivotal trial data cuts are available.

- For manufacturers, not all submissions happen at same time.
- HTAs might:
  - Require resubmissions (e.g., Cancer Drug Fund)
  - Want to go into living HTA direction in case predicted benefits based on immature trial data are uncertain

In the meantime:

- New literature is published.
- Novel costing and pricing information might be available.



What Is Next….

Automated link with local costing and pricing databases

LiveBIM

Programmed in R but functionality to convert to Excel and VBA automatically

Data review + extraction using AI

LiveSTART

LiveSLR™

LiveCEA

LiveNMA

LiveOS

LiveUtility

Pressing one button

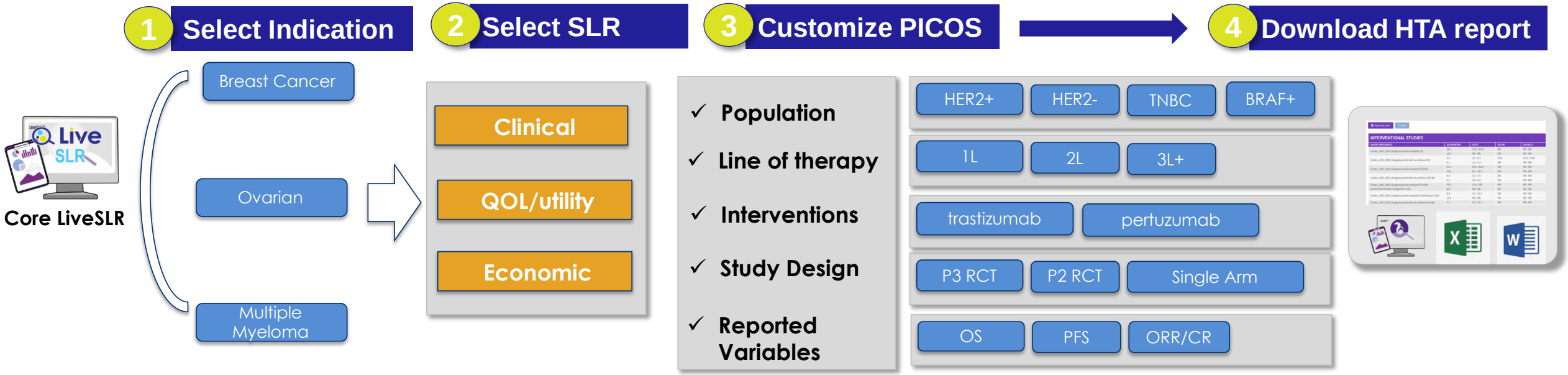
All of these have automated reporting functionality even in local HTA templates

LiveGVD™

LiveHTA™ dossier

LiveSLR - always up-to-date interactive platform

- **High quality, NICE-grade, custom SLRs created using Cochrane + PRISMA methods by trained Cytel Researchers**
- **Once the SLR extraction is completed, its is loaded onto interactive platform and kept up-to-date**
  - Interactive Platform – makes SLRs very user-friendly – ready for analyses
  - Customizable PICOS+ custom online reports – allow for instant creation of custom SLRs for different HTAs
  - Pre-scheduled updates – ensure that SLRs are always ready
  - Monthly congress reviews are loaded into PubTracker – helps tracking competitive intelligence in real time



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Cytel LiveHTA Portal

LiveSLR®

LiveRef™

Your source for current HEOR-related evidence

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annaforsythe@pshta.com

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Follow a simple process to browse and make the selection for different filter parameters to generate custom SLR report

Original studies: 0 matching

Reset filter

1. Select SLR Population

- Demo - PCC 149
- Library - MM Maintenance 208
- Library - MM ND 276
- Library - MM RR 551

2. Select Type of SLR

3. Select Data to Report

You have selected:

No population selected
Please select your population of interest under "Select SLR population" section

View PICOS | View Search Strategy | View PRISMA

Download protocol (No population selected)

Select Data for NMA

Additional User Criteria Selected:

Sub-population: All
Line of therapy: All
Intervention / Comparators: All
Study Design: All
Reported Variables : All

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Original studies: 551 matching | Reset filter

1. Select SLR Population

2. Select Type of SLR

- Interventional 137
- Economic 244
- Quality of Life 62
- Real-world E... 108

3. Select Data to Report

You have selected:

Library - MM RRMM
Relapsed/Refractory Multiple Myeloma

View PICOS | View Search Strategy | View PRISMA

Download protocol (Library - MM RRMM)

Select Data for NMA

Additional User Criteria Selected:

Sub-population: All
Line of therapy: All
Intervention / Comparators: All
Study Design: All
Reported Variables : All

Preview Results (551)

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PICOS and Inclusion-Exclusion Criteria

	PICOS	Inclusion	Exclusion
Patient population	• Patients diagnosed with relapsed/refractory MM	• Patients diagnosed with relapsed/refractory MM	• Non-human • Patients with asymptomatic MM/smoldering MM • Patients with other cancer types
Intervention and Comparators	• Bortezomib • Lenalidomide • Carfilzomib • Ixazomib • Daratumumab • Pomalidomide • Panobinostat • Elotuzumab • Selinexor • Melflufen (melphalan flufenamide) • Vorinostat* • Isatuximab • Bendamustin* • TJ202, MOR202 (felzartamab) • Encorafenib • Binimetinib • Pembrolizumab • Nivolumab • Erdafitinib (JNJ-42756493) • RAPA-201 • Belantamab mafodotin (GSK2857916) • Idecabtagene vicleucel, ide-cel, bb2121 • ciltacabtagene autoleucel, cilta-cel, JNJ-68284528 • CAR-T • Iberdomide • Elranatamab • Teclistamab • Magrolimab	• Bortezomib • Lenalidomide • Carfilzomib • Ixazomib • Daratumumab • Pomalidomide • Panobinostat • Elotuzumab • Selinexor • Melflufen (melphalan flufenamide) • Vorinostat* • Isatuximab • Bendamustin* • TJ202, MOR202 (felzartamab) • Encorafenib • Binimetinib • Pembrolizumab • Nivolumab • Erdafitinib (JNJ-42756493) • RAPA-201 • Belantamab mafodotin (GSK2857916) • Idecabtagene vicleucel, ide-cel, bb2121 • ciltacabtagene autoleucel, cilta-cel, JNJ-68284528 • CAR-T • Iberdomide • Elranatamab • Teclistamab • Magrolimab	• Surgery • Palliative Care • Radiotherapy • Stem Cell Transplantation only • Studies reporting consolidation or maintenance treatment only (without induction) • Studies not including at least one of the interventions listed in the Inclusion Criteria

Search Strategy

Search conducted	Apr 11, 2022
Databases searched	EBM Reviews - Cochrane Database of Systematic Reviews <2005 to April 6, 2022>, EBM Reviews - ACP Journal Club <1991 to March 2022>, EBM Reviews - Database of Abstracts of Reviews of Effects <1st Quarter 2016>, EBM Reviews - Cochrane Clinical Answers <March 2022>, EBM Reviews - Cochrane Central Register of Controlled Trials <March 2022>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <4th Quarter 2016>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2016>, Embase <1974 to 2022 April 08>, Ovid MEDLINE(R) ALL <1946 to April 08, 2022>

	Term	Hits
1	multiple myeloma/	X
2	myeloma/ or multiple myeloma/	X
3	(myeloma$ or multiple-myeloma$ or Kahler$).ti,ab.	X
4	**or/1-3**	**X**
5	exp Recurrence/	X
6	exp cancer recurrence/ or exp relapse/ or exp recurrent disease/	X
7	(relap$ OR refract$ OR resist$ OR persist$ OR return$ OR reoccur$ OR reocur$ OR (re adj2 occur) OR (re adj2 ocur$) OR recurren$ OR salvage$ or RRMM).mp,af,tw.	X
8	(prior or progress$ or (previously adj3 treat$) or (previously adj2 receiv$) or pretreat$ or fail$ or unrespon$).mp,af,tw.	X
9	or/5-8	X
10	**4 and 9**	**X**
11	Bortezomib/ or Lenalidomide/ or Panobinostat/ or Vorinostat/ or Bendamustine Hydrochloride/ or Nivolumab/ or Receptors, Chimeric Antigen/ or Melphalan/ or Leflunomide/ or Azacitidine/ or Dasatinib/ or Crizotinib/ or Afatinib/ or Ado-Trastuzumab Emtansine/ or Ipilimumab/ or B-Cell Maturation Antigen/ or Antibodies, Bispecific/ or Mitoxantrone/	X
12	bortezomib/ or lenalidomide/ or ixazomib/ or daratumumab/ or carfilzomib/ or pomalidomide/ or panobinostat/ or elotuzumab/ or selinexor/ or melphalan flufenamide/ or melphalan/	X
13	vorinostat/ or isatuximab/ or bendamustine/ or belantamab/ or belantamab mafodotin/ or encorafenib/ or binimetinib/ or pembrolizumab/ or nivolumab/ or erdafitinib/ or idecabtagene vicleucel/ or ciltacabtagene autoleucel/ or chimeric antigen receptor/ or iberdomide/ or elranatamab/ or teclistamab/ or magrolimab/ or leflunomide/ or azacitidine/ or talquetamab/ or trametinib/ or dasatinib/ or dabrafenib/ or defactinib/ or binimetinib/ or crizotinib/ or taselisib/ or afatinib/ or capivasertib/ or trastuzumab emtansine/ or ipilimumab/ or nirogacestat/ or mezagitamab/ or B cell maturation antigen/ or bispecific antibody/ or zimberelimab/ or duvelisib/ or venetoclax/ or pirtobrutinib/ or lemzoparlimab/ or eftozanermin alfa/ or cevostamab/ or ciforadenant/ or tasquinimod/ or mitoxantrone/	X
14	(bortezomib or velcade$ or lenalidomide or revlimid$ or revimid$ or ixazomib or ninlaro$ or daratumumab or darzalex$ or carfilzomib or kyprolis$ or pomalidomide or pomalyst$ or imnovid$ or panobinostat or farydak$ or elotuzumab or empliciti$ or selinexor or xpovio$).ti,ab	X
15	(melflufen or melphalan or Merphalan or J1 or J-1 or "J 1" or alkeran$ or evomela$ or PEPAXTO$ or Vorinostat or Zolinza$ or isatuximab$ or Sarclisa$ or bendamustin$ or Bendeka$ or Treanda$ or Belrapzo$ or Ribomustin$ or Cytostasan or TJ202$ or MOR03087 or MOR202$ or Belantamab or BLENREP$ or GSK2857916 or GSK 2857916 or GSK-2857916 or Encorafenib or Braftovi$ or Binimetinib or Mektovi$ or Pembrolizumab or lambrolizumab or Keytruda$ or nivolumab or OPDIVO$ or erdafitinib or Balversa$ or JNJ-42756493 or JNJ42756493 or JNJ 42756493 or Ciltacabtagene Autoleucel or cilta-cel or ciltacel or cilta cel or CARVYKTI$ or JNJ-68284528 or JNJ68284528 or JNJ 68284528 or LCAR-B38M or LCARB38M or LCAR B38M or RAPA-201 or RAPA201 or RAPA 201 or idecabtagene vicleucel or ide-cel or idecel or ide cel or ABECMA$ or bb2121 or bb 2121 or bb-2121).ti,ab.	X

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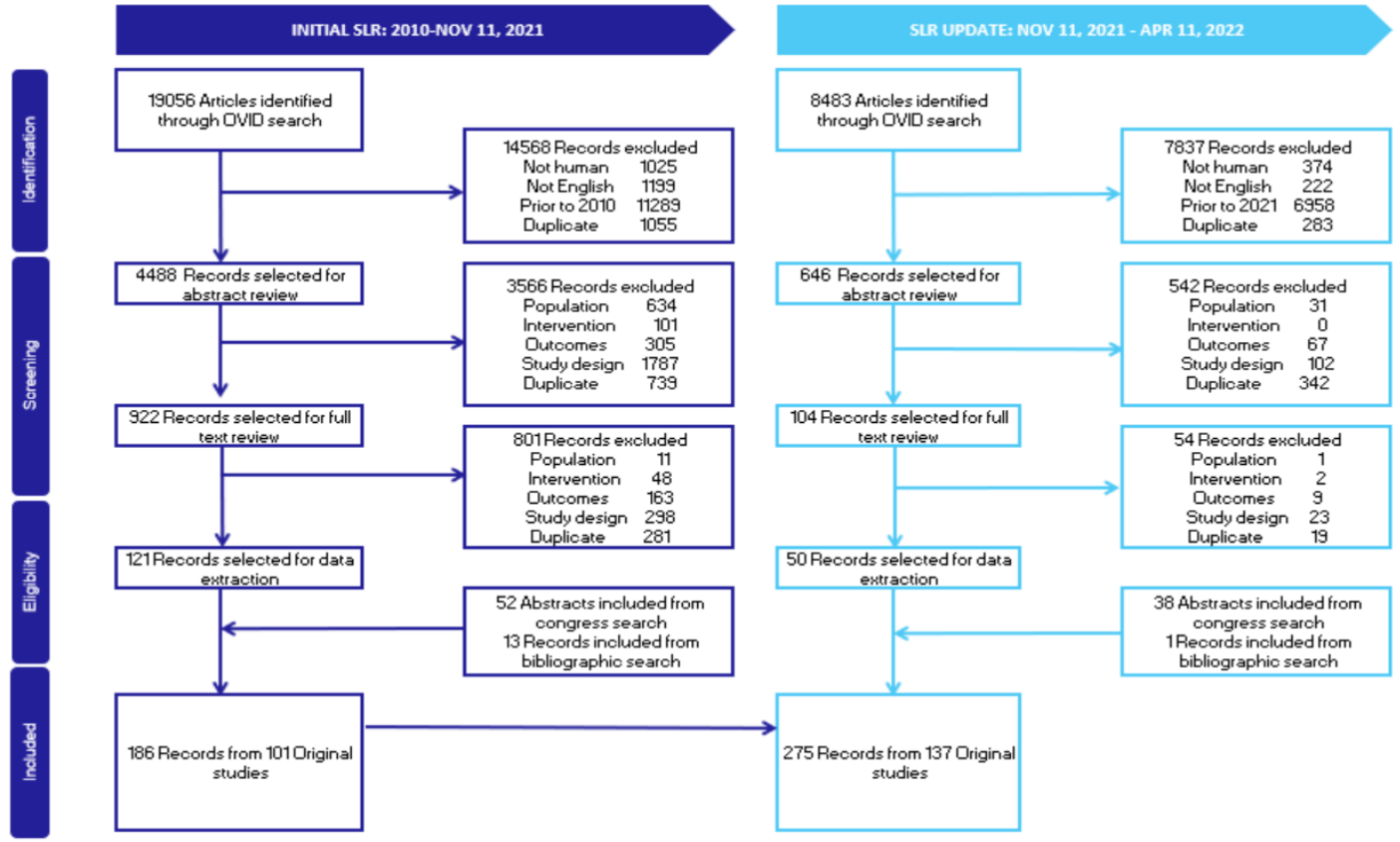

Select Study Design

Select Reported Variables

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Preview Results (137)

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Original studies: 137 matching | Reset filter

1. Select SLR Population
2. Select Type of SLR
3. Select Data to Report

Select additional user criteria (optional):

Select Sub-populations

Select all

Double Refra... 91 | Early RRMM 19 | TRMM 32

Select Line of Therapy
Select Intervention / Comparators
Select Study Design
Select Reported Variables

You have selected:

Library - MM RRMM - Interventional SLR
Relapsed/Refractory Multiple Myeloma

View PICOS | View Search Strategy | View PRISMA

Download protocol (Library - MM RRMM)

Select Data for NMA

Additional User Criteria Selected:

Sub-population: All
Line of therapy: All
Intervention / Comparators: All
Study Design: All
Reported Variables : All

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Select additional user criteria (optional):

Select Sub-populations

Select all

Double Refra... 91 | Early RRMM 19 | TRMM 32

Select Line of Therapy

Select Intervention / Comparators

Select Study Design

Select Reported Variables

Additional User Criteria Selected:

Sub-population: TRMM
Line of therapy: All
Intervention / Comparators: All
Study Design: All
Reported Variables : All

Preview Results (32)

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Updated PRISMA:

Original SLR:	137
Sub-population	-105
Line of therapy	0
Intervention / Comparators:	0
Study Design:	0
Reported Variables :	0
New total selected :	32

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Select additional user criteria (optional):

Select Sub-populations

Select Line of Therapy

Select Intervention / Comparators

Search intervention/comparators

Select all

ALLO-715 (CA... 1	Anti-BCMA (C... 1	Anti-myeloma... 1	ARI0002h (CA... 1
Belantamab m... 3	Carfilzomib 1	CAR-T 2	CART-ddBCMA ... 1
CC-93269 (Bi... 1	Ciltacabtage... 1	CT053 (CAR-T) 1	Daratumumab 1
Dexamethasone 5	Elranatamab ... 1	Elranatamab-... 1	Feladilimab 1
HBI0101 (CAR-T) 1	Idecabtagene... 3	JNJ-64007957... 3	JNJ-64407564... 2
JSMD194 1	Melflufen 2	Modakafusp Alfa 1	Nirogacestat 1
Orvacabtagen... 1	P-BCMA-101 (... 1	Pembrolizumab 1	PF-06863135 ... 1
Pomalidomide 1	REGN5458 (Bi... 1	RG6234 (Bisp... 1	Selinexor 3
TAK-573 1	Talquetamab ... 2	Teclistamab ... 3	TNB-383B (Bi... 1

Additional User Criteria Selected:

Sub-population: TRMM
Line of therapy: All
Intervention / Comparators: All
Study Design: All
Reported Variables : All

Preview Results (32)

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Updated PRISMA:

Original SLR:	137
Sub-population	-105
Line of therapy	0
Intervention / Comparators:	0
Study Design:	0
Reported Variables :	0
New total selected :	32

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Select additional user criteria (optional):

Select Sub-populations

Select Line of Therapy

Select Intervention / Comparators

CAR

Select all

ALLO-715 (CA... 1	Anti-BCMA (C... 1	ARI0002h (CA... 1	Carfilzomib 1
CAR-T 2	CART-ddBCMA .. 1	Ciltacabtage... 1	CT053 (CAR-T) 1
HBI0101 (CAR-T) 1	Idecabtagene... 3	Orvacabtagen... 1	P-BCMA-101 (... 1

Select Study Design

Select Reported Variables

Additional User Criteria Selected:

Sub-population: TRMM

Line of therapy: All

Intervention / Comparators: ALLO-715 (CAR-T) Anti-BCMA (CAR-T) ARI0002h (CAR-T) CAR-T CART-ddBCMA (CAR-T) Ciltacabtagene autoleucel (CAR-T) CT053 (CAR-T) HBI0101 (CAR-T) Idecabtagene vicleucel (CAR-T) Orvacabtagene autoleucel (CAR-T) P-BCMA-101 (CAR-T)

Study Design: All

Reported Variables : All

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Updated PRISMA:

Original SLR:	137
Sub-population	-105
Line of therapy	0
Intervention / Comparators:	-19
Study Design:	0
Reported Variables :	0

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Select additional user criteria (optional):

Select Sub-populations

Select Line of Therapy

Select Intervention / Comparators

Select Study Design

Select Reported Variables

Select all

OS	6	PFS	7	Response	13	Safety	6

Additional User Criteria Selected:

Sub-population: TRMM

Line of therapy: All

Intervention / Comparators: ALLO-715 (CAR-T), Anti-BCMA (CAR-T), ARI0002h (CAR-T), CAR-T, CART-ddBCMA (CAR-T), Ciltacabtagene autoleucel (CAR-T), CT053 (CAR-T), HBI0101 (CAR-T), Idecabtagene vicleucel (CAR-T), Orvacabtagene autoleucel (CAR-T), P-BCMA-101 (CAR-T)

Study Design: All

Reported Variables : All

Preview Results (13)

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Updated PRISMA:

Original SLR:	137
Sub-population	-105
Line of therapy	0
Intervention / Comparators:	-19
Study Design:	0
Reported Variables :	0

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Search LiveSLR™

Follow a simple process to browse and make the selection for different filter parameters to generate custom SLR report

Export as excel | Back

Interventional Report :

Study Characteristics							Patient Characteristics		Efficacy-Survival						
									OS related data						
Article Identifi	Publicatio n Identi	Publicatio n Typ	Short Referenc	Study Title	Intervention (per arm	Intervention (overall	Study N (per arm)	Study N (overal	OS N (per arm)	OS N (overal	OS mont	OS CI	OS HR	OS HR (	OS va
34	114	Original & Update	Lin_ASH_2020a (abstract)	Idecabtagene vicleucel (IDE-CEL, BB2121), a BCMA-directed car t cell therapy, in patients with relapsed and refractory multiple myeloma: Updated results from phase 1 CRB-401 study.	Idecabtagene vicleucel (CAR-T)	Idecabtagene vicleucel (CAR-T)	62	62	62	62	34.2	19.2 - Not Estimable	NR	NR	
59	270	Original & Update	Frigault_ASCO_2022 (abstract)	Phase 1 study of CART-ddBCMA in relapsed or refractory multiple myeloma.	CART-ddBCMA (CAR-T)	CART-ddBCMA (CAR-T)	25	25	24	24	Not Evaluable	NR	NR	NR	
60	155	Original & Update	Manier_JCO_2021 (abstract)	Characteristics of neurotoxicity associated with idecabtagene vicleucel (ide-cel, bb2121) in patients with relapsed and refractory multiple myeloma (RRMM) in the pivotal phase II KarMMa study.	Idecabtagene vicleucel (CAR-T)	Idecabtagene vicleucel (CAR-T)	105	105	105	105	19.4	18 - NR	NR	NR	
60	155	Subgroup	Manier_JCO_2021 (abstract) (with neurotoxicity)	Characteristics of neurotoxicity associated with idecabtagene vicleucel (ide-cel, bb2121) in patients with relapsed and refractory multiple myeloma (RRMM) in the pivotal phase II KarMMa study.	Idecabtagene vicleucel (CAR-T)	Idecabtagene vicleucel (CAR-T)	23	23	23	23	NR	12.3 - NR	NR	NR	
60	47, 48	Original & Update	Munshi_ASCO_2020 (abstract and oral presentation) San Miguel_EHA_2020 (abstract and oral	Idecabtagene vicleucel (ide-cel, BB2121), a BCMA-targeted car T cell therapy, in patients with relapsed and refractory multiple myeloma: Initial karmma results. Idecabtagene vicleucel (ide-cel; bb2121), a	Idecabtagene vicleucel (CAR-T)	Idecabtagene vicleucel (CAR-T)	128	128	128	128	19.4	NR	NR	NR	
60	100, 101	Original	Munshi_NEJM_2021 Anderson_ASCO_2021 (abstract)	Idecabtagene vicleucel in Relapsed and Refractory Multiple Myeloma. Idecabtagene vicleucel (ide-cel, bb2121), a BCMA-directed CAR T cell therapy, in	Idecabtagene vicleucel (CAR-T)	Idecabtagene vicleucel (CAR-T)	128	128	128	128	19.4	18.2 - Not Estimable	NR	NR	

All publications are for review purposes only and may not be distributed internally or externally.

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Pharma client

Safety

Select additional user criteria (optional):

Select Sub-populations

Select Line of Therapy

Select Intervention / Comparators

Select Study Design

Select Reported Variables

Intervention / Comparators: ALLO-715 (CAR-T) Anti-BCMA (CAR-T) ARI0002h (CAR-T) CAR-T CART-ddBCMA (CAR-T) Ciltacabtagene autoleucel (CAR-T) CT053 (CAR-T) HBI0101 (CAR-T) Idecabtagene vicleucel (CAR-T) Orvacabtagene autoleucel (CAR-T) P-BCMA-101 (CAR-T)

Study Design: All

Reported Variables : OS

Preview Results (6)

Generate Complete Excel® Report

Generate complete Word Report

Updated PRISMA:

Original SLR:	137
Sub-population	-105
Line of therapy	0
Intervention / Comparators:	-19
Study Design:	0
Reported Variables :	-7
New total selected :	6

LiveNMA – interactive indirect treatment comparisons tool

Interactive software tool interconnected with LiveSLR and available to all LiveSLR subscribers allows clients to run unlimited number of scenarios in minutes.

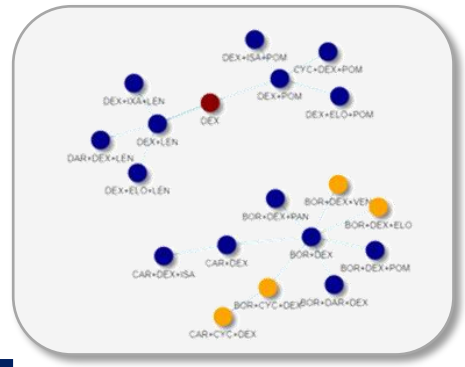
Just 3 easy steps:

1 **Select trials for analysis with specific populations, comparators and outcomes**

Core LiveSLR

SELECT:
- ✓ Indication
- ✓ Sub-populations
- ✓ Comparators
- ✓ Endpoints

2 **View the network and add your own product data based on TPP**



✓ Add your drug based on Target Profile

3 **Run the NMA in seconds; view and download the results as a user-friendly forest plot**

Study	Events (Treatment 1)	Events (Treatment 2)	OR	P(best)
Study 1	36	60	0.58	0.58
Study 2	1	5	0.16	0.16
Study 3	4	11	0.25	0.25
Study 4	14	20	0.70	0.70
Study 5	3	7	0.35	0.35
Study 6	1	7	0.14	0.14
Study 7	8	10	1.02	1.02
Summary			**0.53**	**0.53**

Anna Forsythe
Pharma client

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Search LiveSLR™

Follow a simple process to browse and make the selection for different filter parameters to generate custom SLR report

Original studies: 9 matching | Reset filter

1. Select SLR Population

2. Select Type of SLR

3. Select Data to Report

- [x] Select all
- [ ] Main Message
- [ ] Study Design
- [ ] Population
- [ ] Line of Therapy
- [ ] Patient Characteristics
- [ ] OS-related Data
- [ ] PFS-related Data
- [ ] ORR-related Data
- [ ] Safety

Select additional user criteria (optional):

Select Sub-populations

Select Line of Therapy

You have selected:

Library - MM RRMM - Interventional SLR
Relapsed/Refractory Multiple Myeloma

View PICOS | View Search Strategy | View PRISMA

Download protocol (Library - MM RRMM)

Select Data for NMA

Select NMA Parameters:

- ✔ Interventional SLR
  - ✔ Optional: Sub-population
  - Optional: Line of therapy
  - Optional: Intervention/Comparator
- ✔ Study Design-RCTs Only
- ✔ Reported Variables - OS or PFS

Launch LiveNMA

Additional User Criteria Selected:

Sub-population: Early RRMM
Line of therapy: All
Intervention / Comparators: All

Anna Forsythe
pt_admin

NMA results should be interpreted with caution. Analyses have not been adjusted for potential difference in patient characteristics.
Transitivity, heterogeneity, and consistency assessment strongly recommended

Please contact HEOR team for a full-scope NMA project: livehta-support@cytel.com

Review Studies selected for NMA

OS | PFS

Short Reference	Intervention (Per arm)	Intervention (Abbreviation)	OS N(per arm)	OS HR	OS HR CI Low	OS HR CI High	OS HR p-value	Added to NMA
Siegel_JCO_2018 Stewart_NEJM_2015 (Subgroup 2-3 prior LOT)	Lenalidomide + Dexamethasone	DEX+LEN	NR	NR	NR	NR	NR	✓
	Carfilzomib + Lenalidomide + Dexamethasone	CAR+DEX+LEN	NR	0.73	0.47	1.13	NR	
Siegel_JCO_2018 Stewart_NEJM_2015 (Subgroup 1 prior LOT)	Carfilzomib + Lenalidomide + Dexamethasone	CAR+DEX+LEN	184	0.81	0.62	1.06	NR	✓
	Lenalidomide + Dexamethasone	DEX+LEN	157	NR	NR	NR	NR	
Siegel_JCO_2018 Stewart_NEJM_2015	Lenalidomide + Dexamethasone	DEX+LEN	396	NR	NR	NR	NR	✓
	Carfilzomib + Lenalidomide + Dexamethasone	CAR+DEX+LEN	396	0.79	0.67	0.95	0.0045	

You have selected:

MM RRMM

Selected criteria:

Sub-Population: Early RRMM

Line of therapy: All

Intervention / Comparators: All

Study Design: Phase 2 RCT | Phase 3 RCT

Reported Variables: OS | PFS

+ Add Study Data

Show Network

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Main Navigation

Back to LiveSLR

Data

Network

Result

NMA results should be interpreted with caution. Analyses have not been adjusted for potential difference in patient characteristics.
Transitivity, heterogeneity, and consistency assessment strongly recommended

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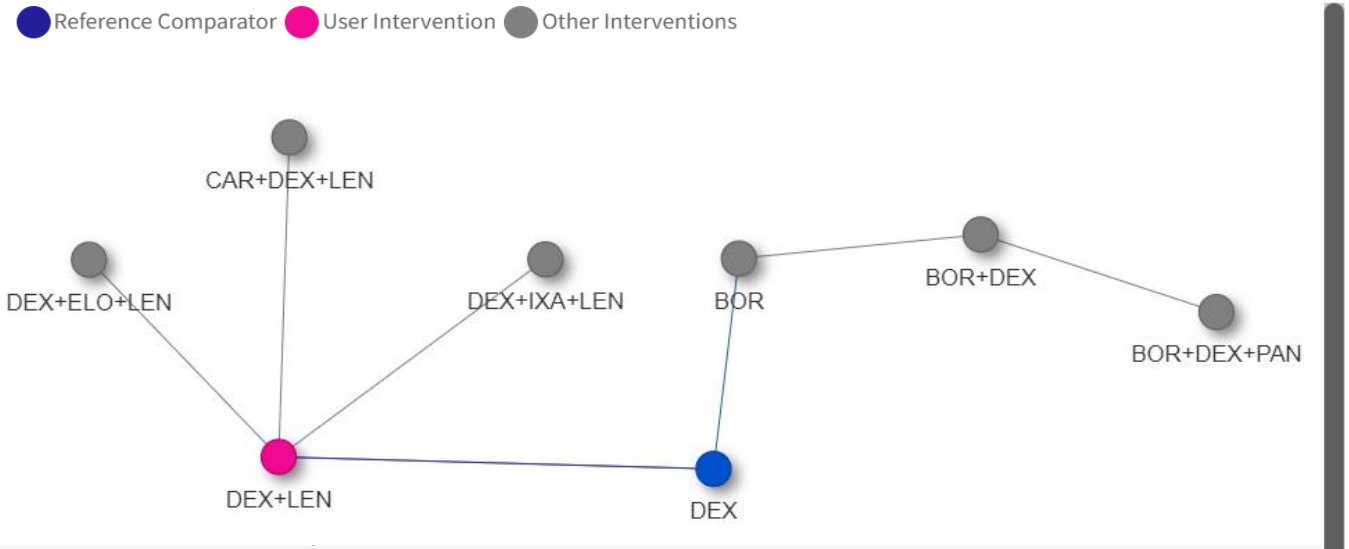
Network

OS | PFS



You have selected:

MM RRMM

Selected criteria:

Sub-Population: Early RRMM

Line of therapy: All

Intervention / Comparators: All

Study Design: Phase 2 RCT | Phase 3 RCT

Reported Variables: OS | PFS

Run NMA

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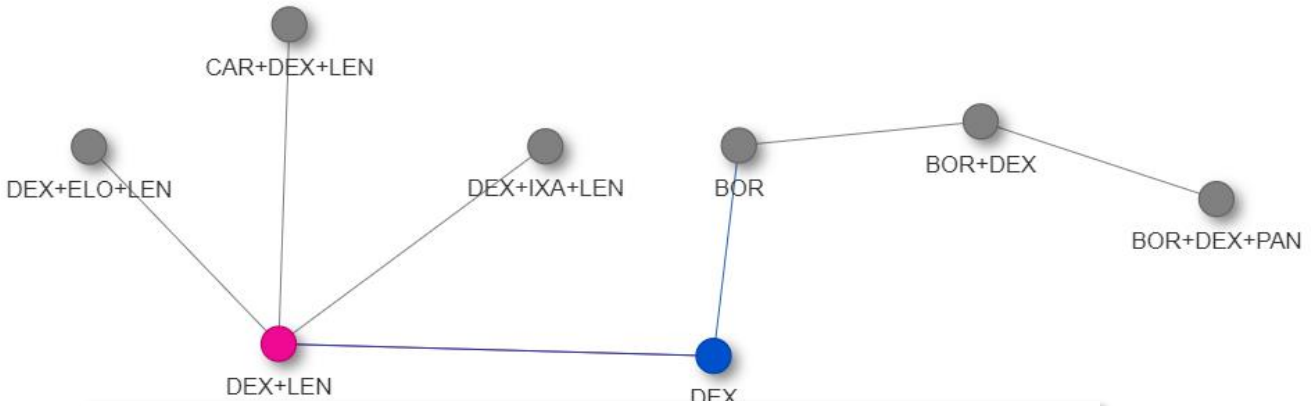
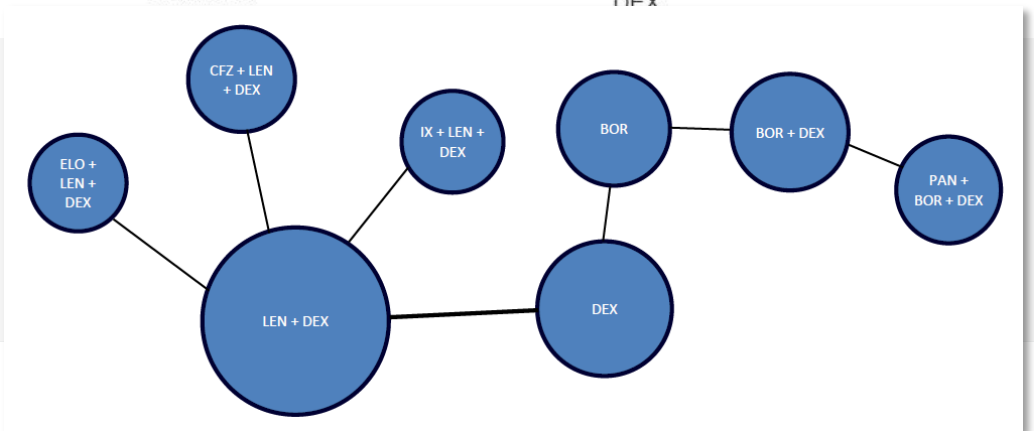
Network

OS PFS

Reference Comparator User Intervention Other Interventions





You have selected:

MM RRMM

Selected criteria:

Sub-Population: Early RRMM

Line of therapy: All

Intervention / Comparators: All

Study Design: Phase 2 RCT Phase 3 RCT

Reported Variables: OS PFS

Run NMA

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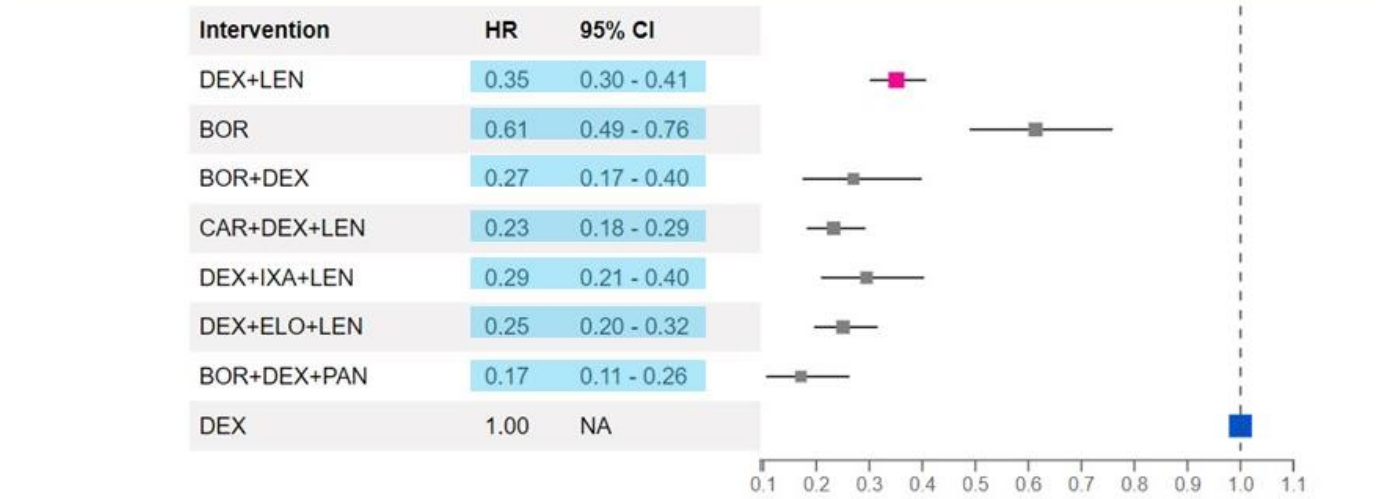
Results: OS

Reference Comparator

Your Intervention

Other Interventions



Short Reference	Intervention (Per arm)	Intervention (Abbreviation)	OS N(per arm)	OS HR	OS HR CI Low	OS HR CI High	OS HR p-value	Added to NMA
Smith_2019	ANN	ANN	200	0.4	0.3	0.7	NR	

You have selected:

MM RRMM

Selected criteria:

Sub-Population: Early RRMM

Line of therapy: All

Intervention / Comparators: All

Study Design: Phase 2 RCT, Phase 3 RCT

Reported Variables: OS, PFS

Print Screen

Cytel LiveNMA™ ≡

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Main Navigation

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Data

Network

Result

NMA results should be interpreted with caution. Analyses have not been adjusted for potential difference in patient characteristics.

Transit

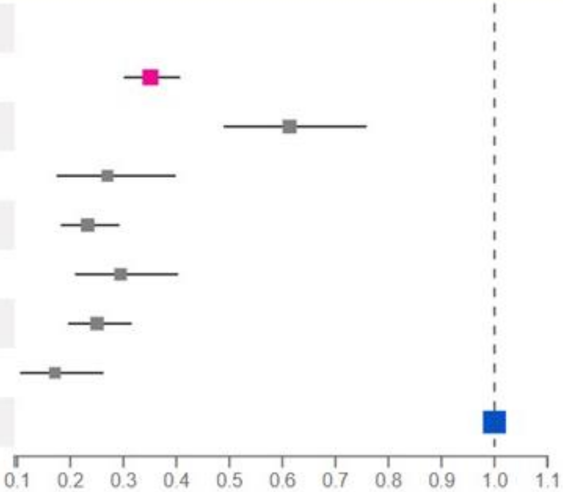
Please

Results

FE Model:
resdev, 6.996 vs. 8;
DIC = -4.288

PAN BOR DEX							
0.78 (0.41 to 1.51)	CFZ LEN DEX						
0.77 (0.40 to 1.50)	0.99 (0.75 to 1.30)	ELO LEN DEX					
0.73 (0.37 to 1.44)	0.93 (0.69 to 1.26)	0.95 (0.70 to 1.28)	IX LEN DEX				
0.58 (0.48 to 0.71)	0.74 (0.39 to 1.39)	0.75 (0.40 to 1.41)	0.80 (0.42 to 1.52)	BOR DEX			
0.54 (0.29 to 1.02)	0.69 (0.57 to 0.83)	0.70 (0.57 to 0.86)	0.74 (0.59 to 0.93)	0.93 (0.51 to 1.71)	LEN DEX		
0.34 (0.20 to 0.60)	0.44 (0.31 to 0.62)	0.45 (0.31 to 0.64)	0.47 (0.32 to 0.69)	0.59 (0.35 to 1.01)	0.64 (0.47 to 0.86)	BOR	
0.19 (0.10 to 0.35)	0.24 (0.18 to 0.32)	0.25 (0.19 to 0.32)	0.26 (0.19 to 0.35)	0.33 (0.18 to 0.58)	0.35 (0.29 to 0.42)	0.55 (0.44 to 0.69)	DEX

Intervention	HR	95% CI
DEX+LEN	0.35	0.30 - 0.41
BOR	0.61	0.49 - 0.76
BOR+DEX	0.27	0.17 - 0.40
CAR+DEX+LEN	0.23	0.18 - 0.29
DEX+IXA+LEN	0.29	0.21 - 0.40
DEX+ELO+LEN	0.25	0.20 - 0.32
BOR+DEX+PAN	0.17	0.11 - 0.26
DEX	1.00	NA



Short Reference	Intervention (Per arm)	Intervention (Abbreviation)	OS N(per arm)	OS HR	OS HR CI Low	OS HR CI High	OS HR p-value	Added to NMA
Smith_2019	ANN	ANN	200	0.4	0.3	0.7	NR	

You have selected:

MM RRMM

Selected criteria:

Sub-Population: Early RRMM

Line of therapy: All

Intervention / Comparators: All

Study Design: Phase 2 RCT | Phase 3 RCT

Reported Variables: OS | PFS

Print Screen

WordReport-Libr....docx

Show all

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Main Navigation

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Data

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Result

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Transitivity, heterogeneity, and consistency assessment strongly recommended

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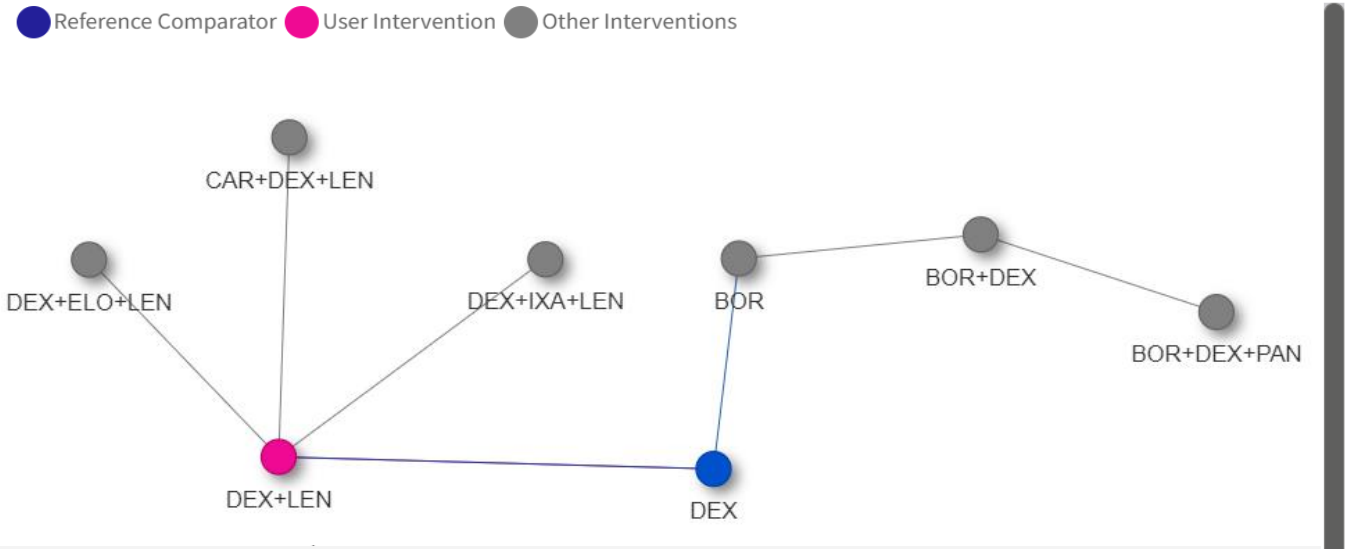
Network

OS | PFS



You have selected:

MM RRMM

Selected criteria:

Sub-Population: Early RRMM

Line of therapy: All

Intervention / Comparators: All

Study Design: Phase 2 RCT | Phase 3 RCT

Reported Variables: OS | PFS

Run NMA

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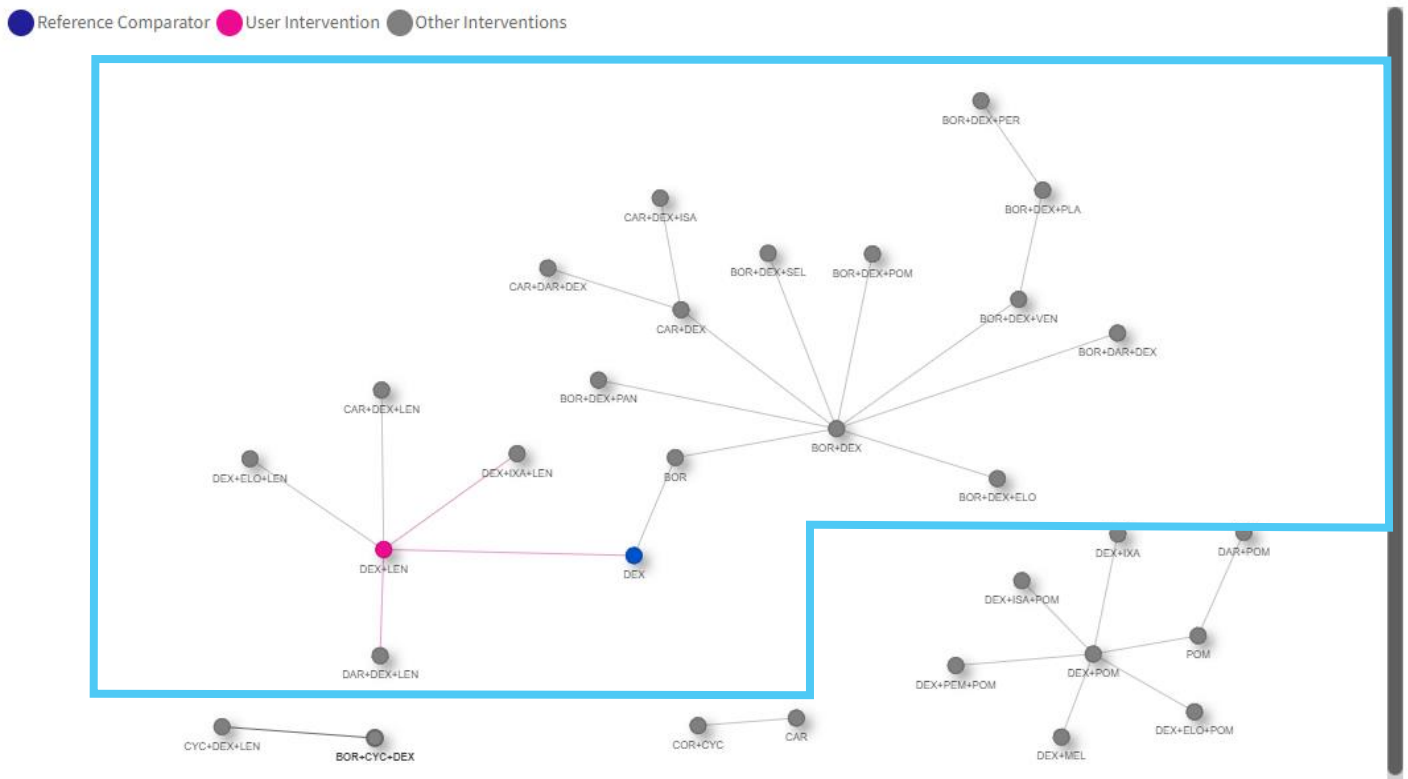
Network

OS | PFS



You have selected:

MM RRMM

Selected criteria:

Sub-Population: Early RRMM

Line of therapy: All

Intervention / Comparators: All

Study Design: Phase 2 RCT | Phase 3 RCT

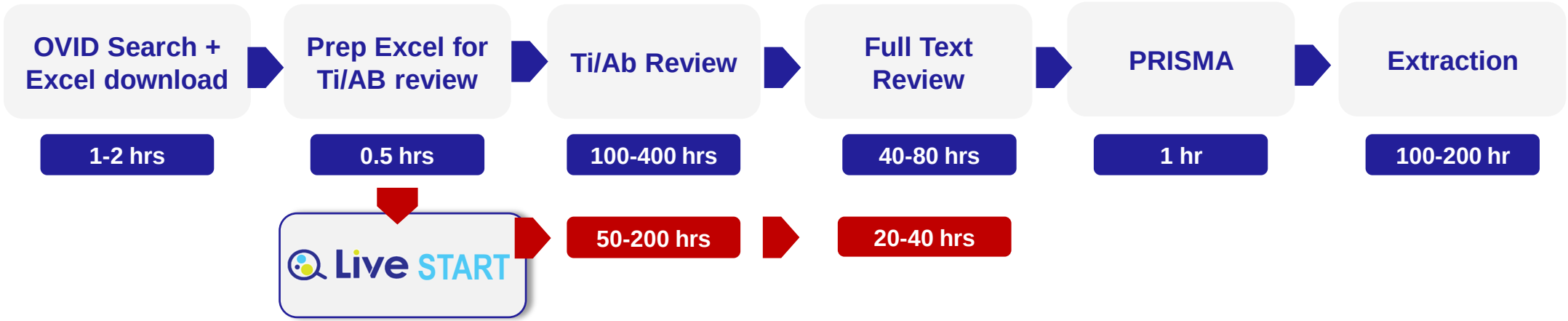
Reported Variables: OS | PFS

Run NMA

LiveStart

Background:

- One of the key challenges is how to systematically review an increasingly higher volume of evidence while ensuring unbiased and timely decisions are made for the assessment of new technologies
- Title & Abstract review and initial extraction of key data to aid the selection of relevant articles, are the most time consuming and capacity limiting portions of any SLR
- It has been suggested that the HTA processes should be enhanced using technological advances. Meanwhile, the new PRISMA guidelines[1] does not prohibit the inclusion of automated tools in screening



- Cytel developed an AI tool, LiveSTART, utilizing transfer learning to perform the title and abstract (TiAb) review as well as extraction of key data to aid in SLR process Page MJ, McKenzie JE, Bossuyt PM, et al.

1. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi:10.1136/bmj.n71

LiveSTART – 3 easy steps

Cytel LiveSTART™

1 Download template for PICOS & Title/Abstract Review files

Download Template

2 Choose spreadsheet file

Choose file

Import Spreadsheet

3

Uploading

Reviewing

Download Review

LiveSTART – Output

- LiveSTART output files are immediately ready for use in a Microsoft Excel format
- LiveSTART conducts hierarchical review on every PICOS criteria across all records
- Reason for rejection is accompanied by selected text from the abstract used to make the decision

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
1	ORN	DB	PT	AU	SO	TI	AB	Shortened AB	Duplicate group #	Population probability	Intervention probability	Study design probability	Outcome probability	Predicted Selection	Predicted Reason for Rejection	Comment	Selection	Reason for Rejection
2	143	CCTR	Journal: Conferen	Burger JA, Sivina	Blood. Vol.130,	Randomi zed trial	Backgrou nd: Single		26	1		0.98	0.99	YES				
3	199	CCTR	Conferen ce	Burger JA, Sivina	Blood. Conferen	Randomi zed trial	Backgro nd:		26				0.99	N				
4	140	CCTR	Journal: Conferen	Salles G, Smolej L,	Blood. Vol.130,	Single- agent	uct	PFS and OS outcomes	25				0.04	N				
5	196	CCTR	Conferen ce	Salles G,	Blood.	Si	ntroduct		25				0.02	N				
6	139	CCTR	Jou Co				u		4	0.98	0.98	0.93	0.97	Y				
7	195	CCTR	Co ce				u			0.98	0.98	0.91	0.97	N				
8	138	CCTR	Jou Co				ct	Pts are randomized		0.98	1	0.01	0.94	NO	STUDY DESIGN			
9	194	CCTR	Conferen ce	Davids MS,	Blood. Conferen	Initial results of	Introduct ion			0.98	1	0.01	0.94	NO	DUPLICATE	ORN# 138		
10	132	CCTR	Journal: Conferen	Soumerai JD, Ni A,	Blood. Vol.130,	A validated	Intro ion:			1	1	0.04	0.96	NO	STUDY DESIGN			
11	188	CCTR	Conferen ce	Soumerai JD, Ni A,	Blood. Conferen	A validated	Intro ion:			1	1	0.04	0.96	NO	DUPLICATE	ORN# 132		
12	131	CCTR	Journal: Conferen	Lockmer S,	Blood. Vol.130,	Long- term	Back nd: F			0	1	0.99	0.99	NO	POPULATION			
13	187	CCTR	Conferen ce	Lockmer S,	Blood. Conferen	Long- term	Back nd: For		21	0	1	0.99	0.99	NO	DUPLICATE	ORN# 131		
			Journal:	Eyre TA,	Blood.	Idelalisib-	Backgrou	Background:										

AI-Shortened Abstract
Sentences that can be used to validate the AI decision

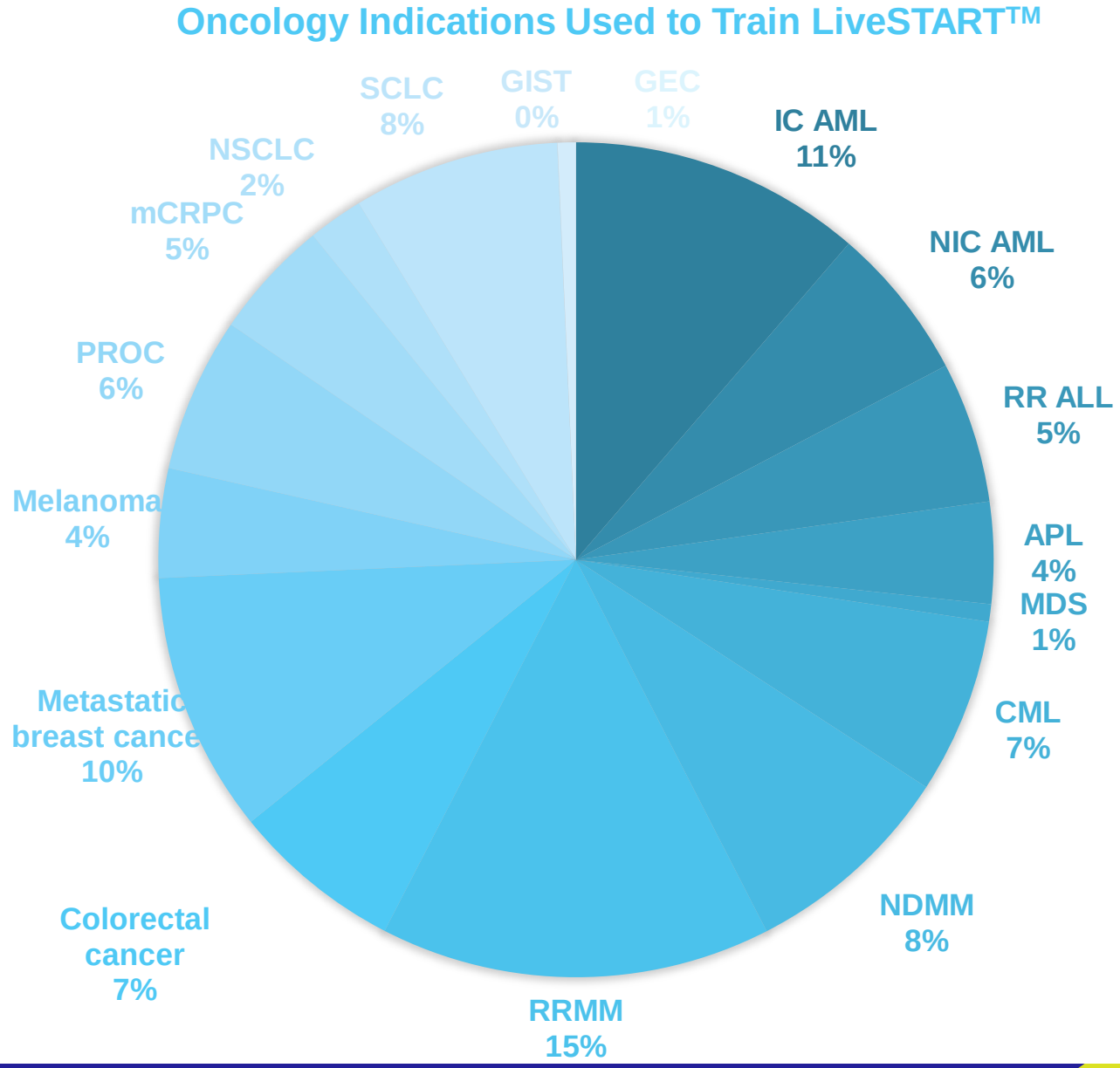
Groups of duplicates
Citations with the same ID belong to the same duplicate groups

AI prediction of probability of inclusion by each PICOS criteria

AI's decision of inclusion/exclusion
Reason of rejection is based on the pre-selected hierarchy
Comment includes the duplicate ID

LiveSTART - Methods

- AI was trained with annotated SLR datasets, prepared by two separate reviewers
- **59 annotated datasets** were used
  - 51 oncology
- **Type of SLRs:**
  - 47 clinical
  - 6 economic and
  - 6 HRQOL SLRs



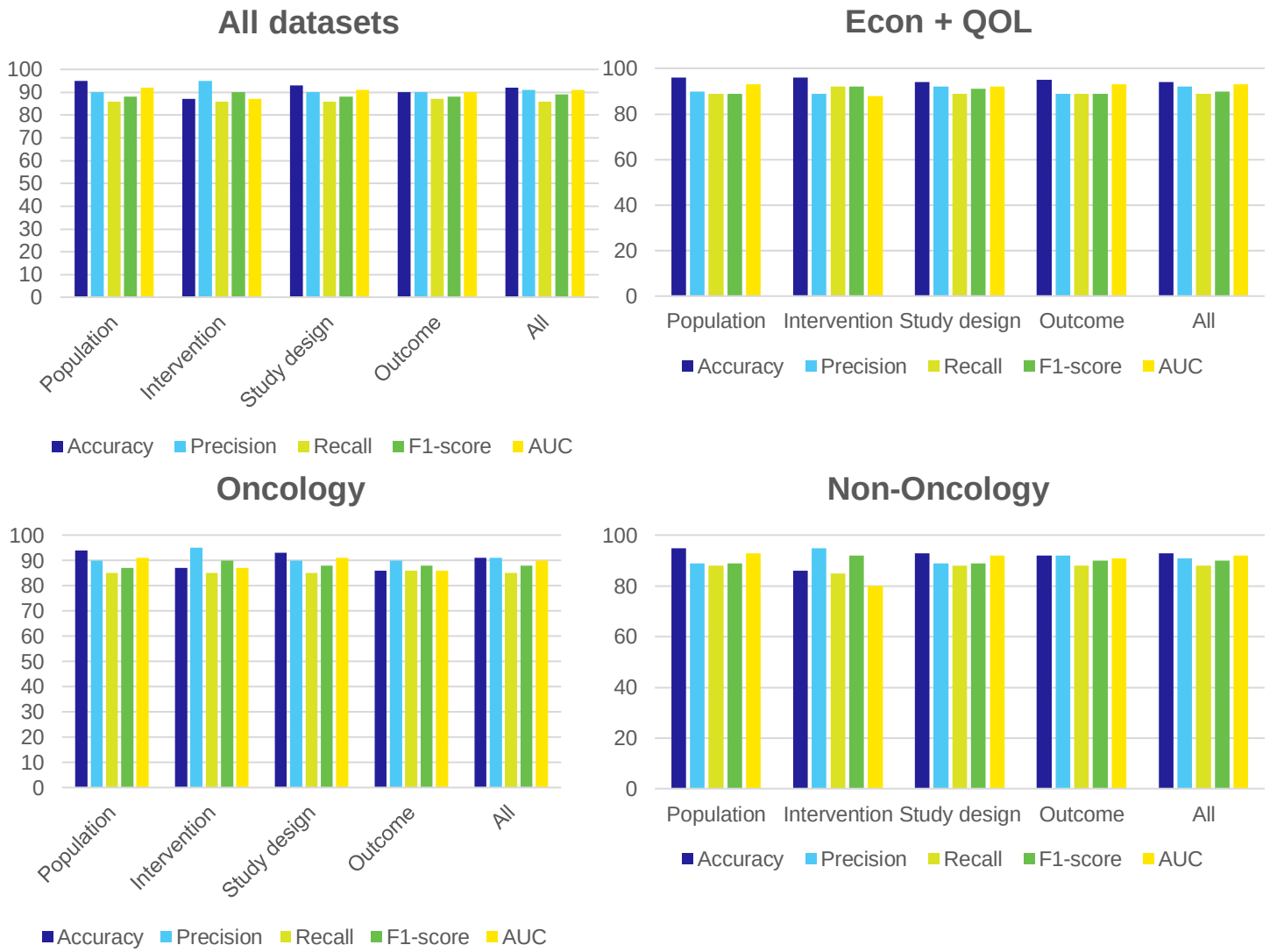
LiveSTART – Accuracy

- Validation showed:
  - an overall accuracy = 0.92
  - precision = 0.91
  - recall = 0.86

  when compared to the results generated by two independent reviewers and a third verifier.

- LiveSTART™ reviews 1000 publications in ≈10 minutes with no additional preparation of the datasets as compared to manual review

LiveSTART™ Validation by Evidence or Indication Type

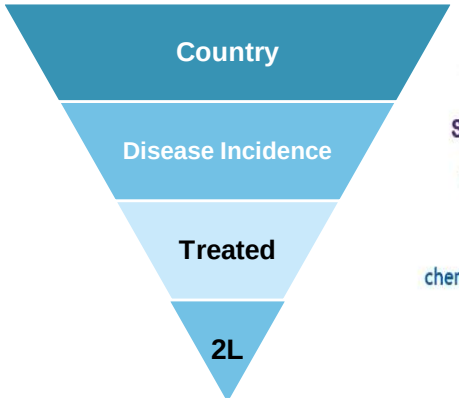


LiveBIM

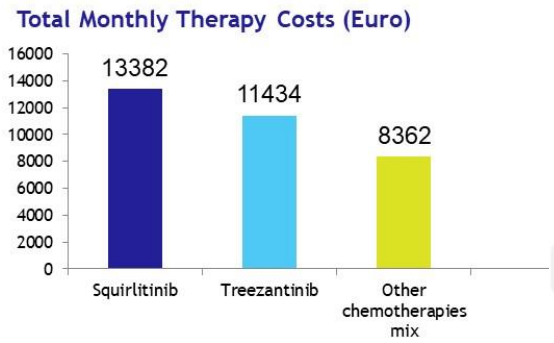
Background:

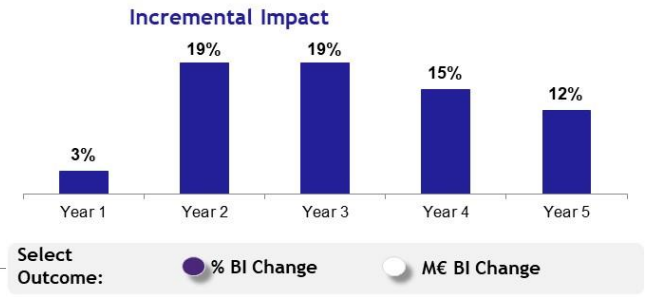
- Budget Impact Models (BIM) have a structured approach
- This allows for standardization and automation
- LiveBIM provides a user-friendly dashboard where users follow the flow to build up a BIM step by step
- Inputs can be inserted manually or taken from LiveSLR or cost databases
- When ready, the BIM can be discussed through the dashboard with colleagues or clients
- Exported to Excel and Word for a HTA-ready model and report

Epidemiology → Market Shares → Costs → Results



Treatment	Year 1	Year 2	Year 3	Year 4	Year 5
Squirlitinib	21%	32%	26%	19%	16%
Walnutnib	32%	28%	22%	18%	16%
Other chemotherapies	47%	40%	52%	62%	69%
Total	100%	100%	100%	100%	100%





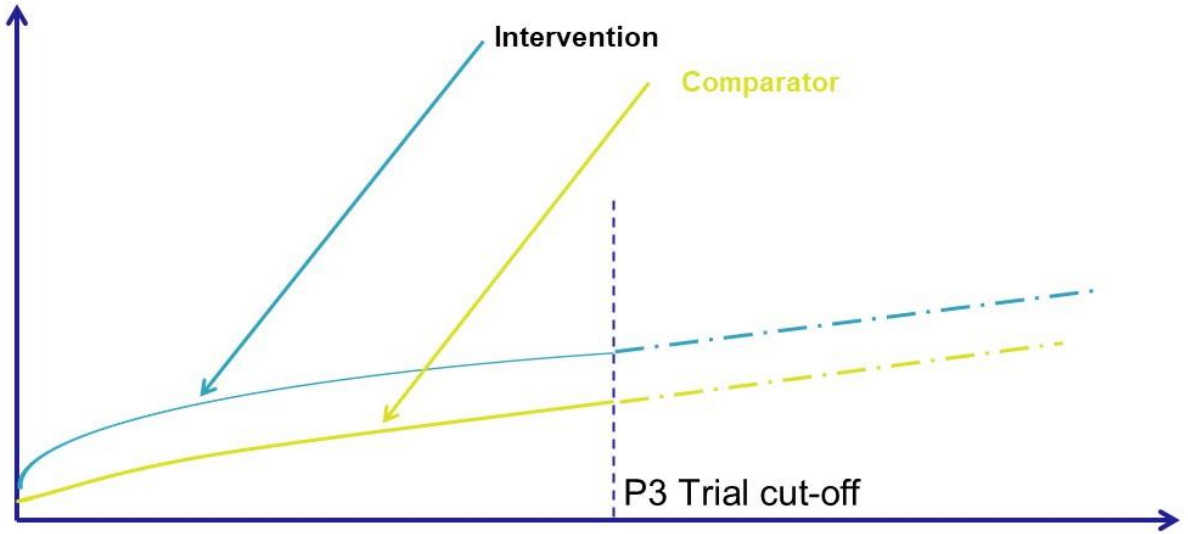
LiveOS - Standardizing survival analyses

Background

- Cost-effectiveness models for the treatment of long-term conditions often require information on effectiveness beyond the period of available data
- Most HTAs require data extrapolation to long terms (10 years and lifetime)
- Various statistical models must be used to extrapolate data beyond pivotal trials

LiveOS

- LiveOS combines the programming of statistical analyses with an intuitive interface
- Allows users to analyze and comment the data simultaneously
- Generates the reporting in Word
- Export the results to Excel for easy implementation in economic models



Thank you.

Feel free to contract: anna.forsythe@cytel.com

Cytel