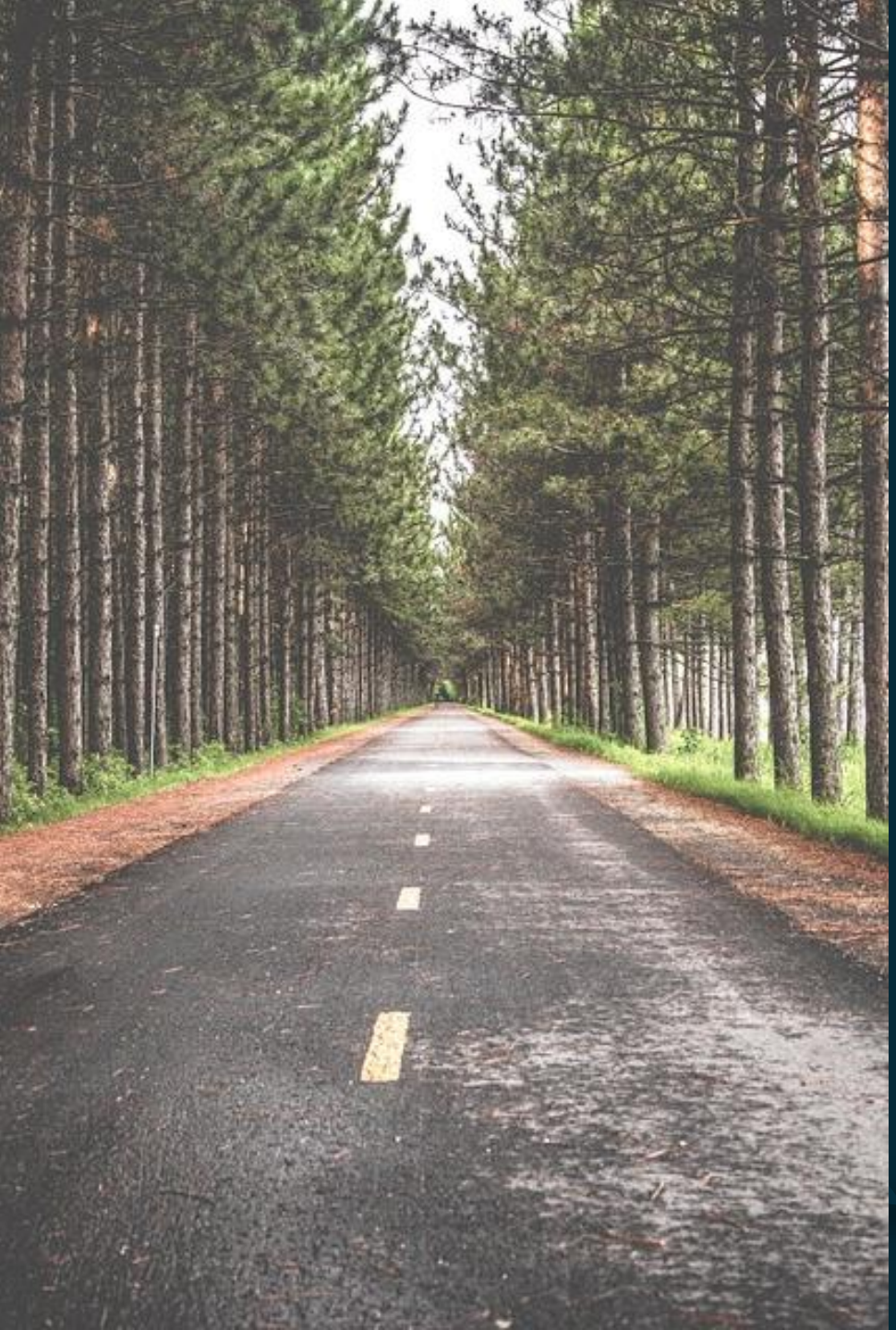
End to End Standards driven Oncology Studies

Kevin Lee, Director of Data Science
at Clindata Insight



The Agenda

- Introduction of Oncology
- Why Standards?
- Oncology-specific Standards: Subtype, Response Criteria guideline, Data Collection, CDISC, Analysis
- Standards-driven Oncology Studies
- Final Thoughts / Q&A

Cancer Facts

- The word ‘cancer’ is related to the Greek word “crab” because its finger-like projections were similar to the shape of the crab
- In 2010, the economic cost of the disease worldwide was estimated at $1.16 trillion.
- One in eight deaths in the world are due to cancer.
- WHO predicts new cancer cases of 14 million in 2012 to 22 million in 2030 and cancer deaths from 8.2 million a year to 13 million annually.
- Men who are married are up to 35% less likely to die from cancer than those who are not married.

FDA CDER NMEs and BLAs Approval

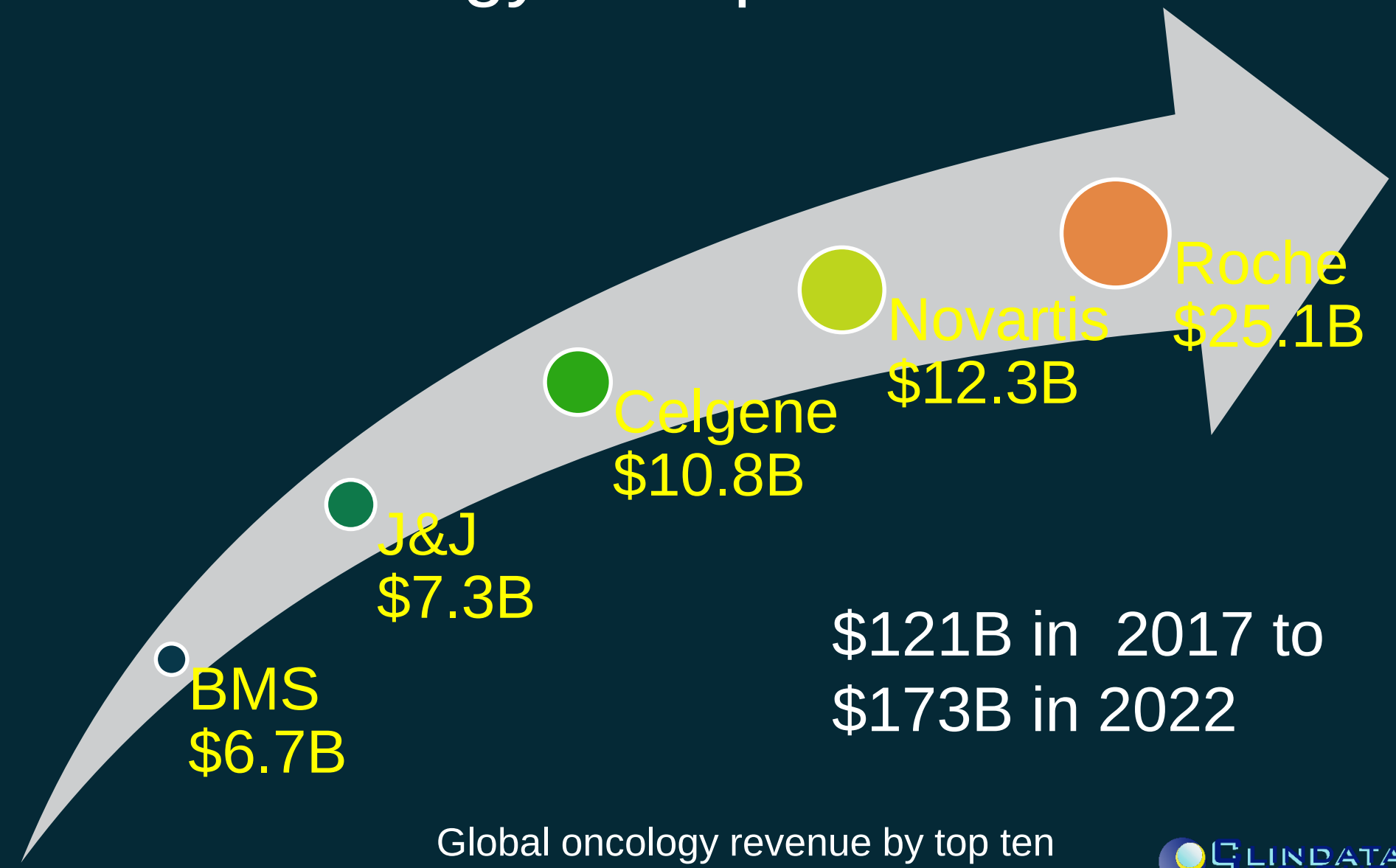
- 2012 - 39 Approval, 13 Oncology (33 %)
- 2013 - 27 Approval, 8 Oncology (30 %)
- 2014 - 41 Approval, 9 Oncology (22%)
- 2015 - 45 Approval, 13 Oncology (29%)
- 2016 – 22 Approval, 6 Oncology (27%)
- 2017 – 46 Approval, 12 Oncology (26%)

Note: based on the reports of **NMEs and BLAs approved by CDER**

Many Pharma Companies Turns their Focus to Cancer

- A cornerstone to the success
- Unmet medical needs
- Profitable

TOP Oncology Companies



$121B in 2017 to
$173B in 2022

Global oncology revenue by top ten pharmaceutical companies 2017

We live in the **oncology** drug development environment.

What do we feel about oncology studies?

- Different
- Complex
- Difficult

Difference in Oncology Studies

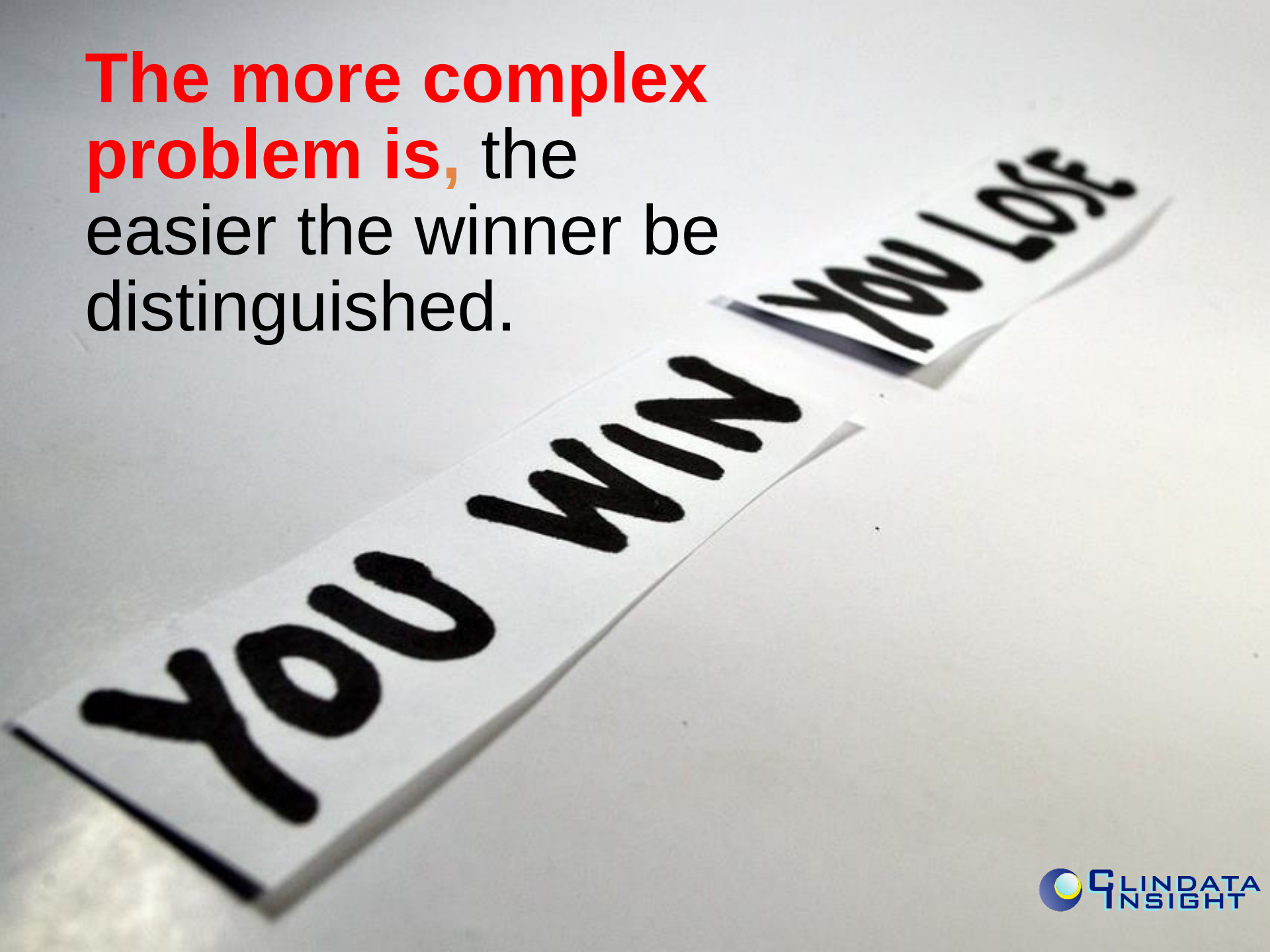
- Tumor measurements and their response to drug
- Oncology-specific measurements for response criteria (e.g., Liver and Spleen Enlargement, Bone Marrow Infiltrate and Blood Counts)
- Oncology-diagnosis measurements (e.g., immunophenotype, performance status by ECOG, stage)
- Toxicity (Lab and AE)
- Time to Event Analysis (e.g., OS, PFS, TTP and ORR, Kaplan Meier Curves)


Houston,
we have a
BIG
Challenge!!!

How to scale infrastructures for more oncology studies

How to conduct complex oncology studies

The more complex problem is, the easier the winner be distinguished.



GLINDATA INSIGHT

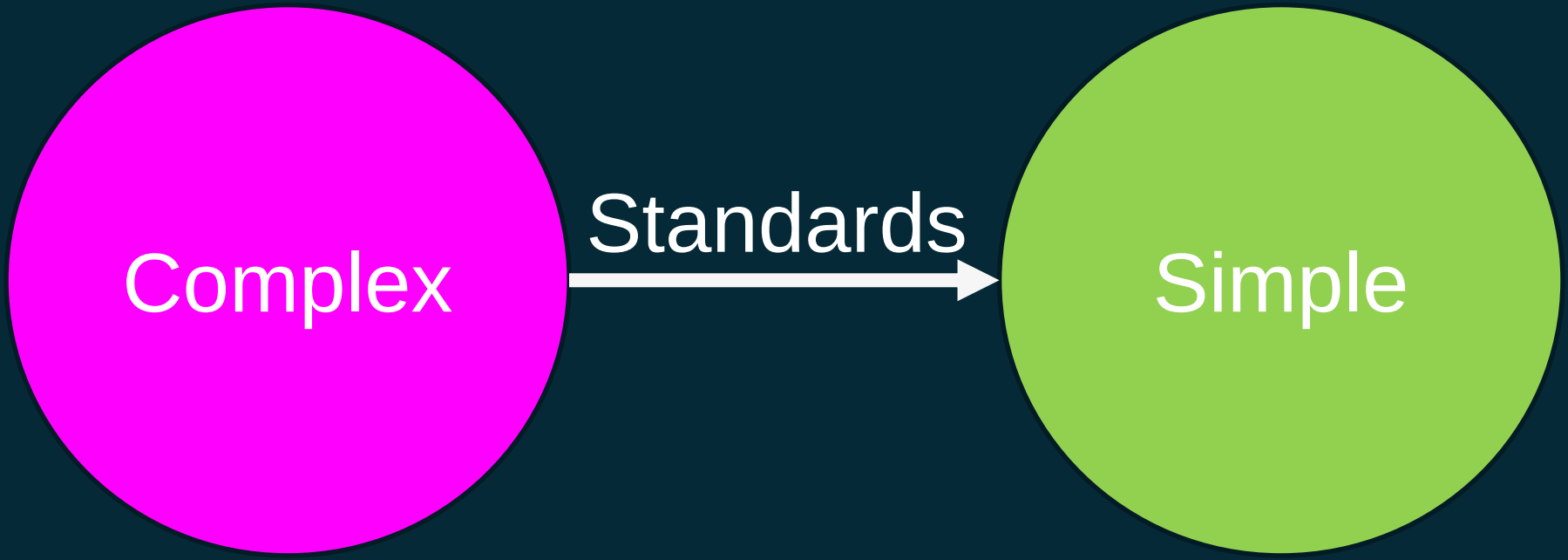
Complex problem for 6th grader

If (x + 2) = 1000,
what is $x^2 - 4 =$?

x = 1000 – 2 = 988

$988^2 - 4 =$

How can we solve the complex problem?



Oncology-specific Standards

- Study Sub-type
- Response Criteria Guidelines
- CDISC
- Analysis

Oncology specific Standards

Study Subtype

- Oncology clinical trial study types

Response Criteria Guideline

- What to collect
- How to measure tumor
- How to determine responses

CDISC

- How to store/submit the data

Analysis

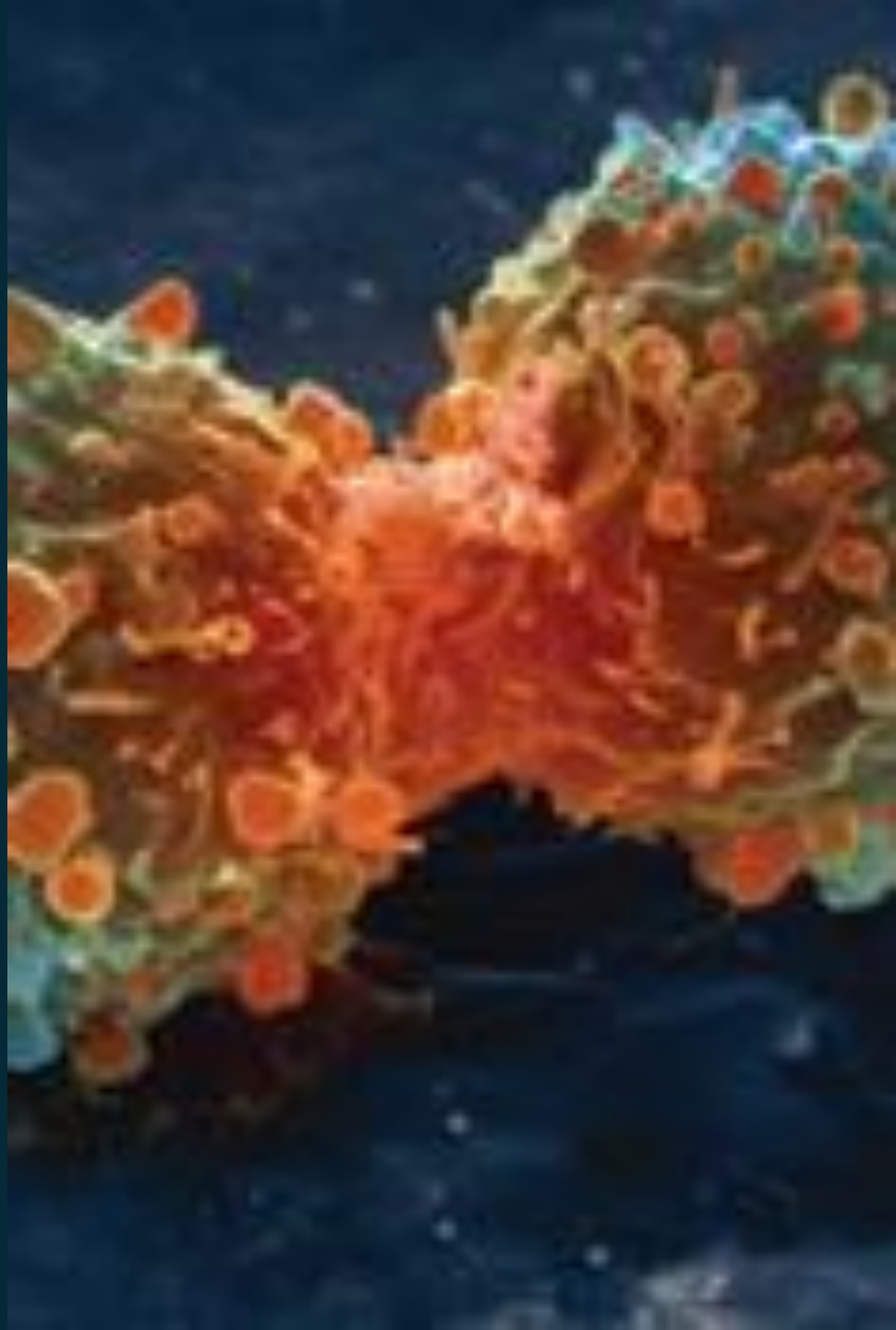
- How to analyze/report the data

Oncology Study Subtypes

- Solid Tumor
- Lymphoma
- Leukemia

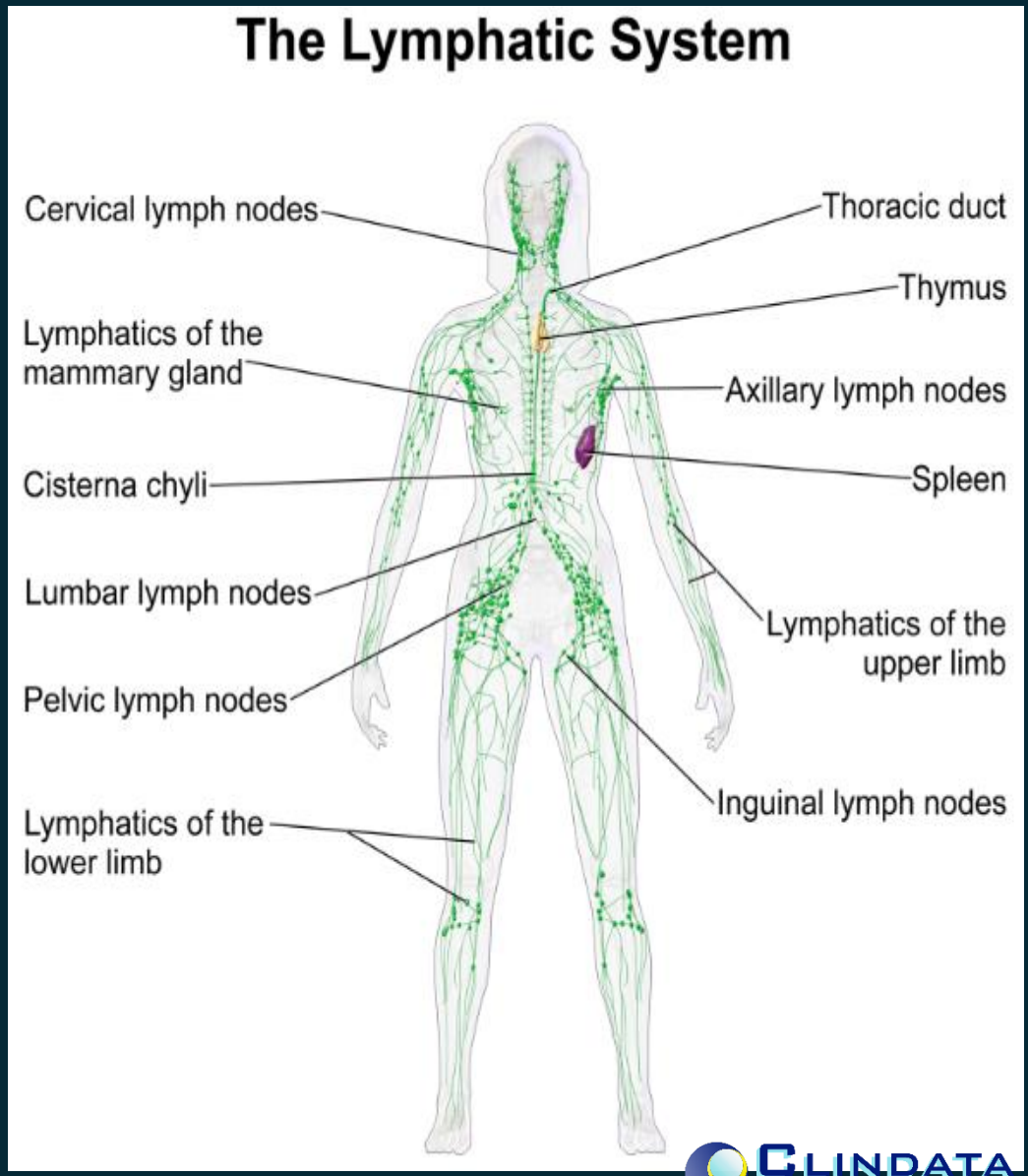
Solid Tumor

- An abnormal mass of tissue that are not cysts or liquid
- Most common
- Type – breast, prostate, lung, liver and pancreatic cancer and melanoma



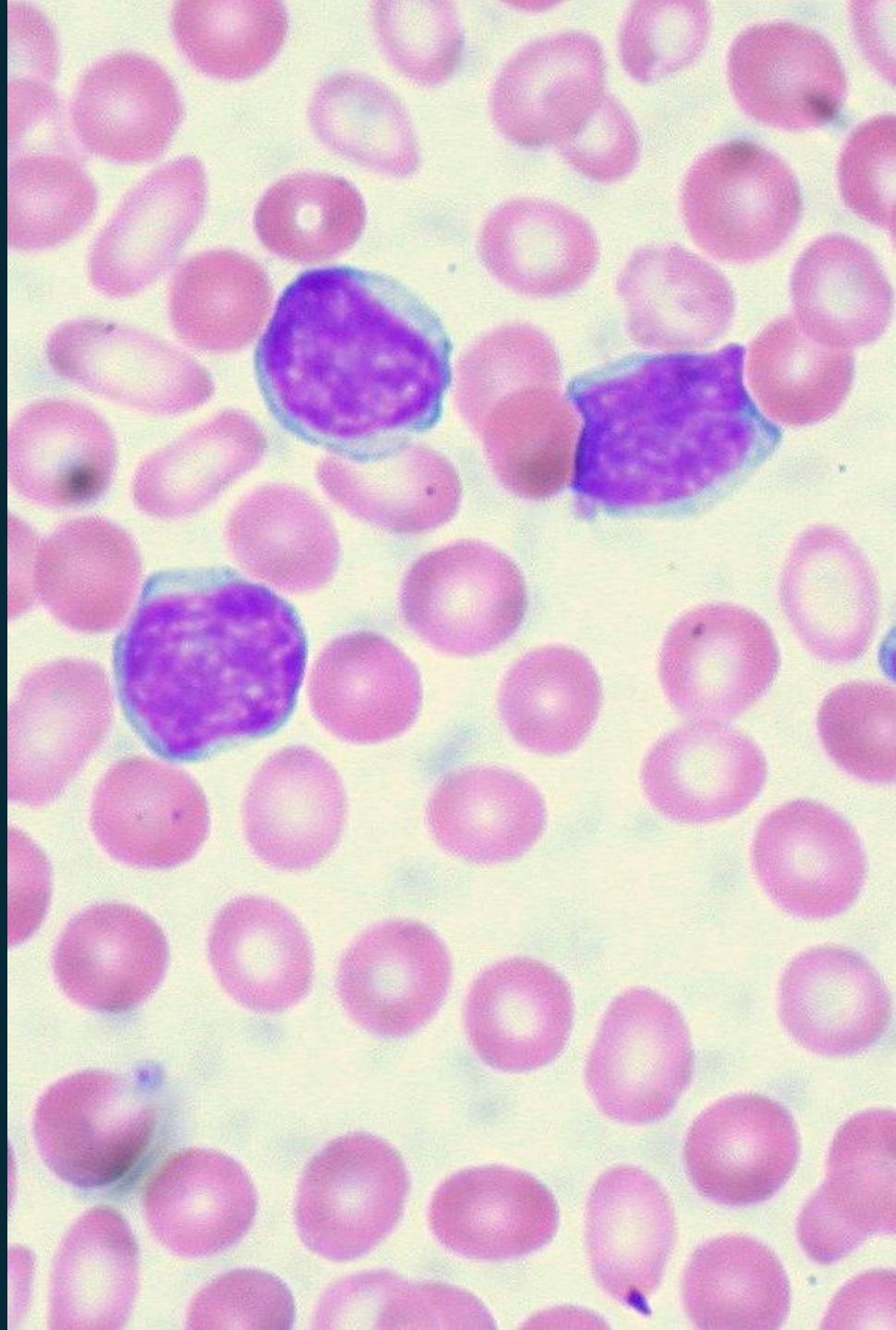
Lymphoma

- Cancer that starts in Lymph Node
- Tumor types:
  - Enlarged Lymph Node
  - Nodal Mases
  - Extra Nodal Masses



Leukemia

- Cancer that usually begins in the bone marrow and result in high number of WBC
- Types:
  - Chronic Lymphocytic Leukemia(CLL)
  - Chronic Myeloid Leukemia(CML)
  - Acute Lymphoblastic Leukemia (ALL)
  - Acute Myeloid Leukemia (AML)



Response Criteria Guidelines

Solid Tumor

- RECIST (Response Evaluation Criteria in Solid Tumor) 1.1
- irRC(Immune-related Response Criteria) 2009

Lymphoma

- Cheson 2007
- Cheson 2014 (2014 Lugano classification)

Leukemia

- IWCLL 2008
- IWAML 2003
- NCCN Guideline 2012 on ALL
- CML ESMO Guidelines

CDISC Oncology specific Standards

- CDASH
- SDTM
  - TU : Tumor Identification
  - TR : Tumor Results
  - RS : Response
- ADaM
  - -TTE : Time to Event Analysis Datasets

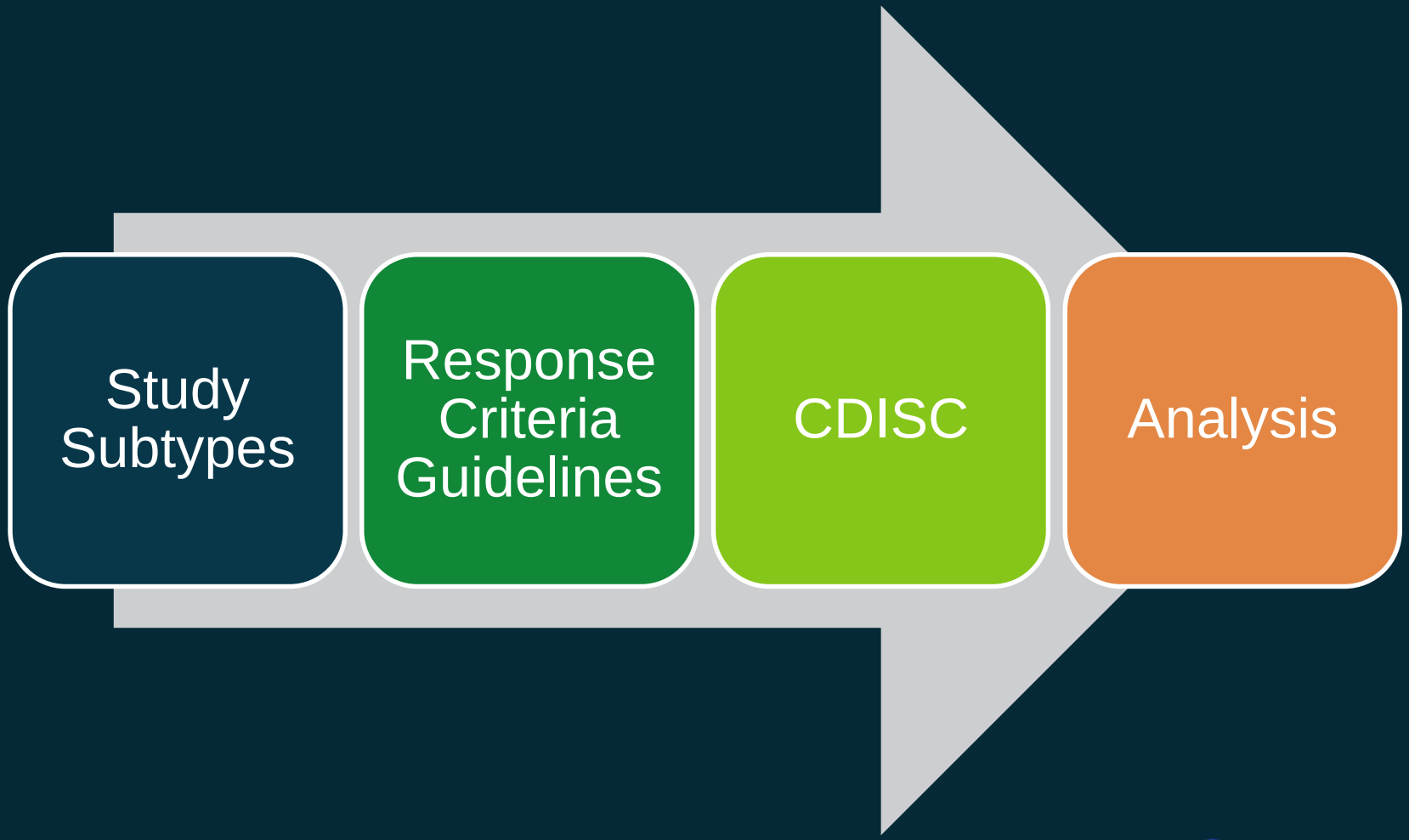
CDISC Oncology specific Standards

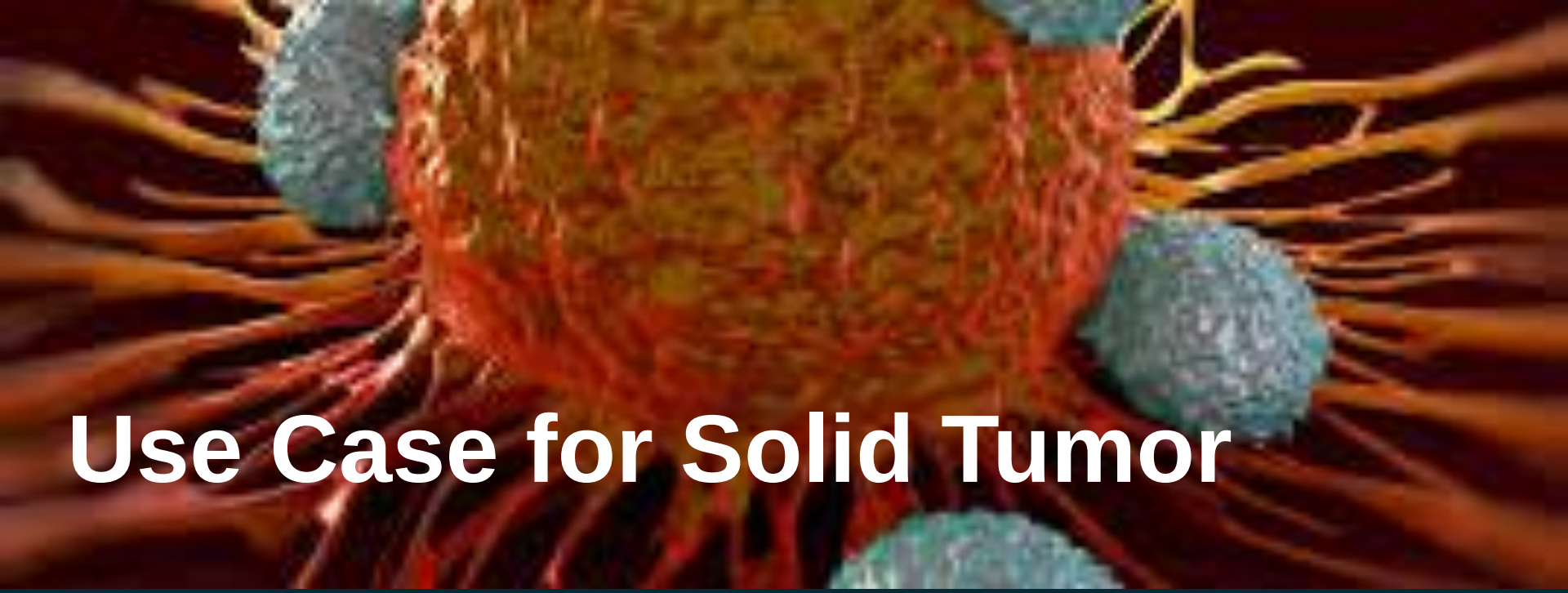
- CT
  - Response Criteria : CR, PR, PD, SD, irCR, irPR, irPD, irSD
  - Tumor Measurements : LDIAM, SUMDIA, LPERP, AREA, SUMAREA, TUMSTATE
  - Response : TRGRESP, NTRGRESP, NEWLPROG, OVRLRESP, BESTRESP

Oncology specific **Analysis**

- OS – Overall Survival
- PFS – Progression Free Survival
- ORR – Objective Response Rate

Standards Implemented Oncology Studies

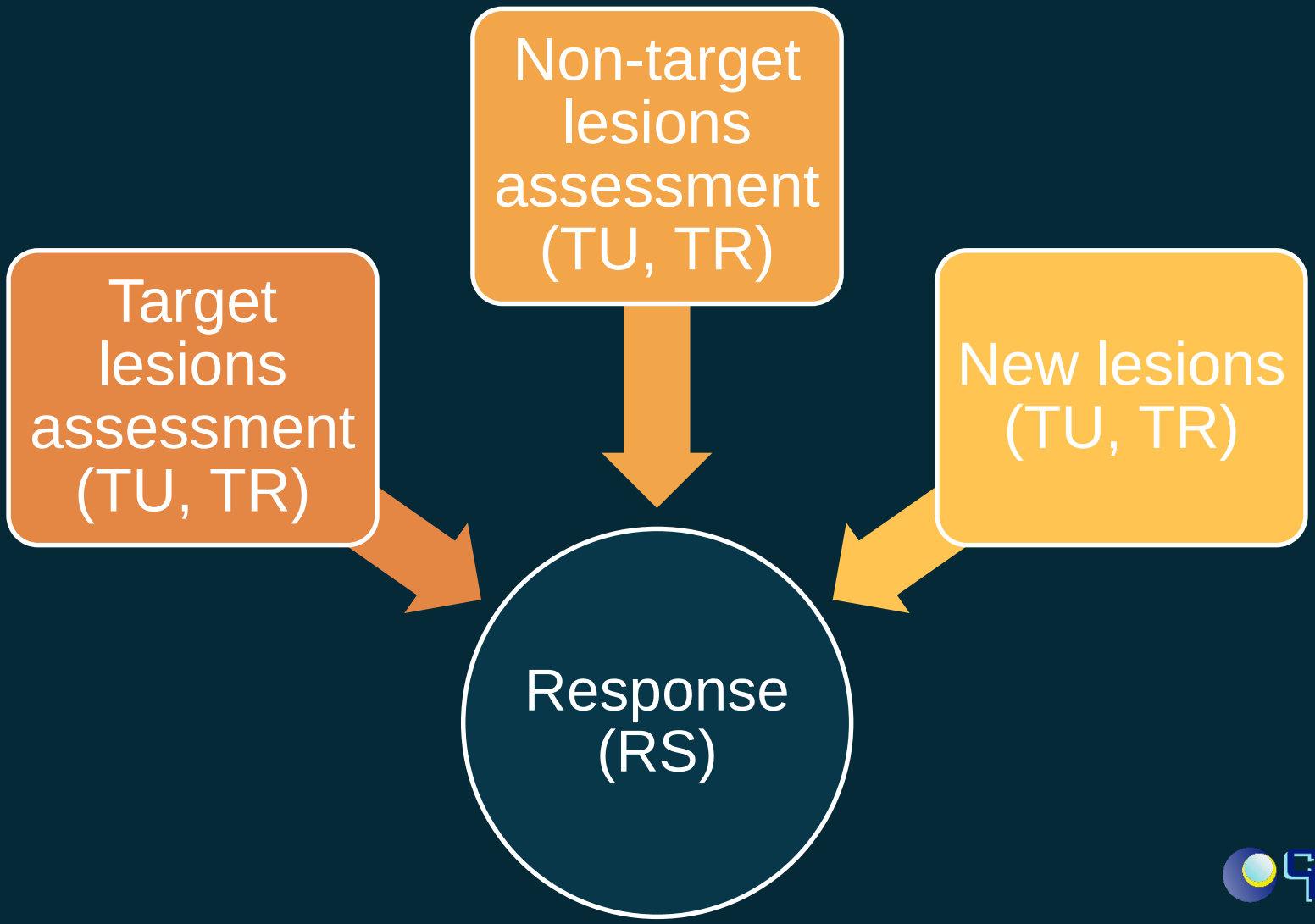




Use Case for Solid Tumor

Solid Tumor → RECIST 1.1 → Tumor Collection

RECIST 1.1 based data collections and response measurements



CDISC SDTM TU based on RECIST 1.1 data collection

USUBJID	TULINKID	TUTESTCD	TUTEST	TUORRES	TULOC	TUMETHOD	VISIT
001-01-001	T01	TUMIDENT	Tumor Identification	TARGET	ABDOMEN	CT SCAN	Cycle 1
001-01-001	T02	TUMIDENT	Tumor Identification	TARGET	ABDOMEN	CT SCAN	Cycle 1
001-01-001	T03	TUMIDENT	Tumor Identification	TARGET	THYROID	CT SCAN	Cycle 1
001-01-001	NT01	TUMIDENT	Tumor Identification	NON-TARGET	LIVER	CT SCAN	Cycle 1
001-01-001	NT02	TUMIDENT	Tumor Identification	NON-TARGET	KIDNEY	CT SCAN	Cycle 1
001-01-001	NT03	TUMIDENT	Tumor Identification	NON-TARGET	SPLEEN	CT SCAN	Cycle 1

Key points to note:

- Subject 001 has 3 target and 3 non-targets at Cycle 1
- TU.TULINKID is connected TR.TRLINKID using RELREC.

CDISC SDTM TR based on RECIST 1.1 data collection

USUBJID	TRGRPID	TRLINKID	TRTESTCD	TRTEST	TRCAT	TRORRES	TRORRESU	VISIT
001-01-001	Target	T01	LDIAM	Longest Diameter	Measurement	10	mm	Cycle 1
001-01-001	Target	T02	LDIAM	Longest Diameter	Measurement	10	mm	Cycle 1
001-01-001	Target	T03	LDIAM	Longest Diameter	Measurement	15	mm	Cycle 1
001-01-001	Target		SUMDIAM	Sum of Diameter	Measurement	35	mm	Cycle 1
001-01-001	Non-Target	NT01	TUMSTATE	Tumor State	Qualitative	PRESENT		Cycle 1
001-01-001	Non-Target	NT02	TUMSTATE	Tumor State	Qualitative	PRESENT		Cycle 1
001-01-001	Non-Target	NT03	TUMSTATE	Tumor State	Qualitative	PRESENT		Cycle 1

- Sum of Diameter changed from 70 mm to 35 mm
- No changes in non-target.
- No new lesion

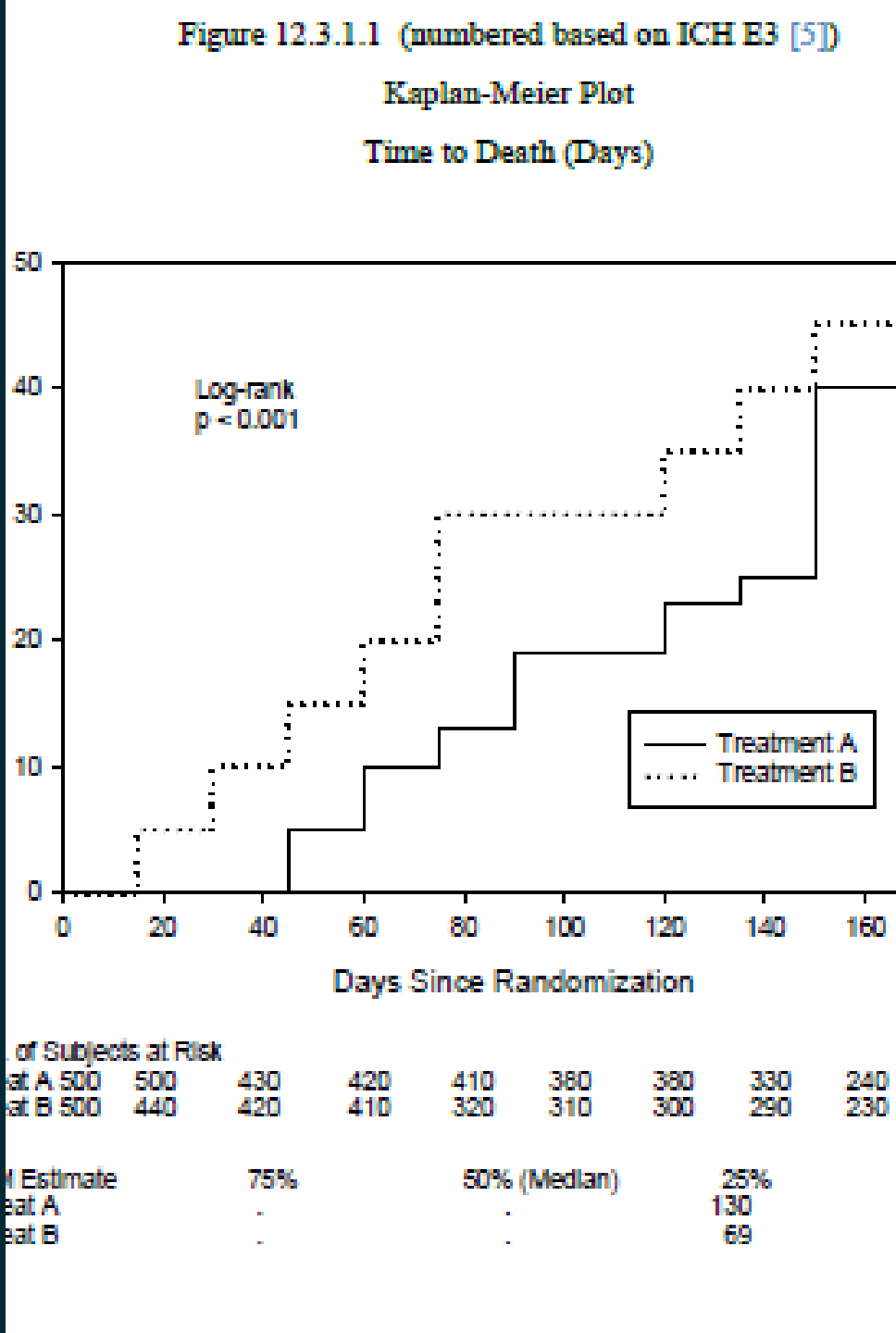
Response Assessment at Cycle 1 for RECIST 1.1 (TR to RS)

USUBJID	TRGRID	TRLINKID	TRTESTCD	TRTEST	TRORRES	TRORRESU	VISIT
001-01-001	Target	T01	LDIAM	Longest Diameter	10	mm	Cycle 1
001-01-001	Target	T02	LDIAM	Longest Diameter	10	mm	Cycle 1
001-01-001	Target	T03	LDIAM	Longest Diameter	15	mm	Cycle 1
001-01-001	Target		SUMDIAM	Sum of Diameter	35	mm	Cycle 1
001-01-001	Non-Target	NT01	TUMSTATE	Tumor State	PRESENT		Cycle 1
001-01-001	Non-Target	NT02	TUMSTATE	Tumor State	PRESENT		Cycle 1
001-01-001	Non-Target	NT03	TUMSTATE	Tumor State	PRESENT		Cycle 1

USUBJID	RSTESTCD	RSTEST	RSCAT	RSORRES	VISIT
001-01-001	TRGRESP	Target Response	RECIST 1.1	PR	Cycle 1
001-01-001	NTRGRESP	Non-target Response	RECIST 1.1	NonCR/NonPD	Cycle 1
001-01-001	NEWLPROG	New Lesion Progression	RECIST 1.1	N	Cycle 1
001-01-001	OVRLRESP	Overall Response	RECIST 1.1	PR	Cycle 1

Oncology Specific Efficacy **Time to Event** Analysis

- Time to Event ADaM datasets
- OS – Overall Survival
- PFS – Progression Free Survival
- Kaplan Meier Curves



Time to Event Analysis in ADaM

USUBJID	TRTP	PARAM	AVAL	START DT	ADT	CNSR	EVNTDESC
001-01-001	Study Drug 1	Time to Death (Days)	157	2011-01-04	2011-06-10	1	COMPLETED THE STUDY
001-01-002	Study Drug 2	Time to Death (Days)	116	2011-02-01	2011-05-28	1	LOST TO FOLLOW-UP
001-01-003	Study Drug 2	Time to Death (Days)	88	2011-02-05	2011-05-04	0	DEATH
001-01-004	Study Drug 1	Time to Death (Days)	102	2011-03-20	2011-06-30	1	ONGOING
001-01-005	Study Drug 1	Time to Death (Days)	101	2011-03-26	2011-07-05	1	ONGOING

Overall Survival analysis by Kaplan Meier plot, log rank test or Cox Regression Analysis.

Standards Driven automated Oncology Studies

CDISC

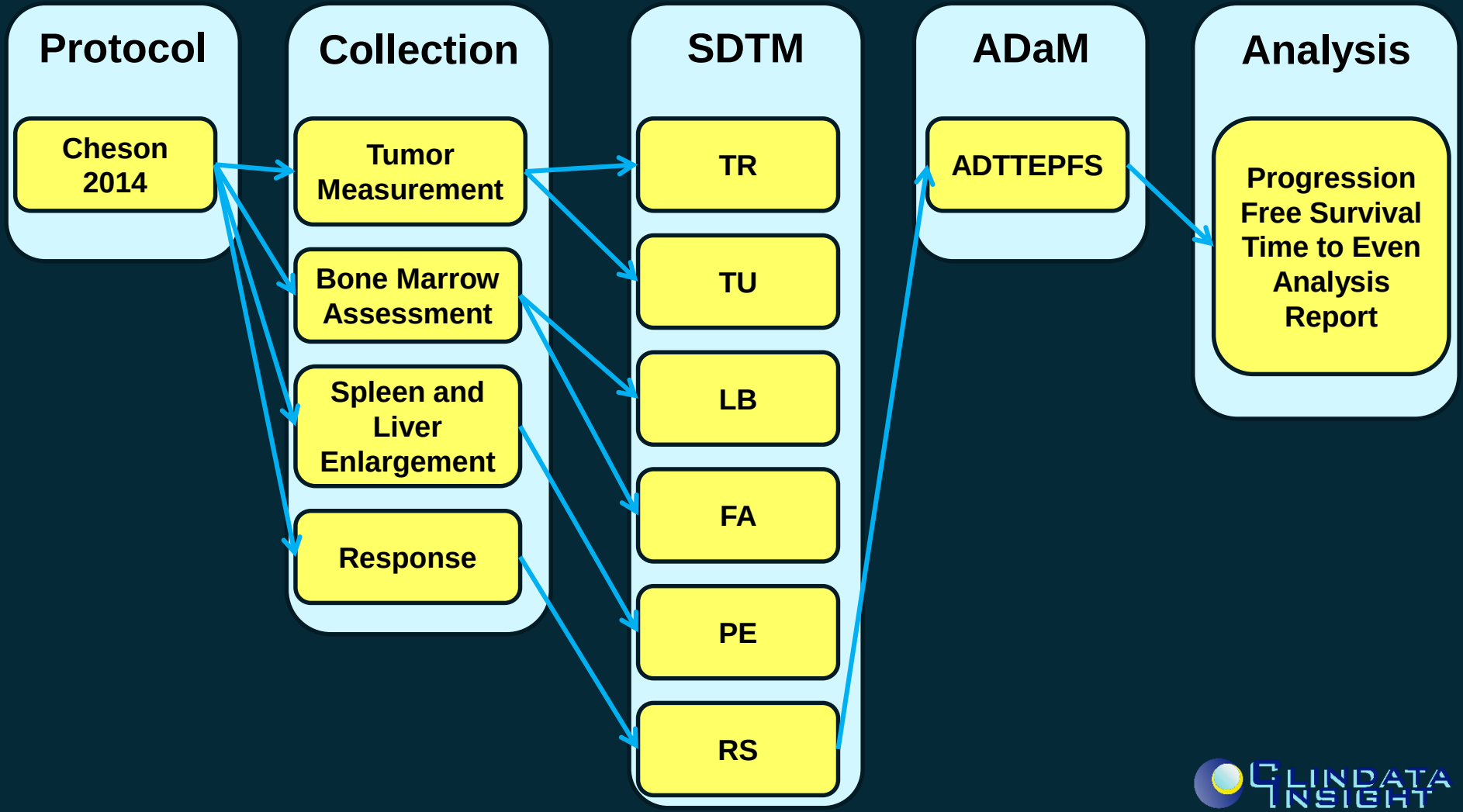
Response Criteria

Analysis

Oncology-specific Standards Library

- **Response Criteria Guidelines**
  - RECIST 1.1
  - Cheson 2014
  - IWCLL 2008
- **Collection**
  - Tumor Measurement
  - Bone Marrow Assessment
  - Spleen and Liver Enlargement Assessment
  - Blood Counts
  - Response Assessment
- **CDISC**
  - SDTM : TU, TR, RS
  - ADaM : --TTE
  - CT : CR, PR, PD, SD, irCR, irPR, irPD, irSD, LDIAM, SUMDIA, LPERP, AREA, SUMAREA, TUMSTATE, TRGRESP, NTRGRESP, NEWLPROG
- **Analysis**
  - OS, PFS,TTP, ORR, DFS
  - Reporting – Tables, Listings and Graphs
  - SAS Macros / R Packages
  - Algorithms (Industry, Company)
- **Documents**
  - Links
  - Traceability
  - Trainings
  - SOP / WG

E2E Standards-driven automated process of Oncology Study



Why Standards driven process in oncology studies?

- Regulatory compliance
- Easy to understand
- Scalable
- 20/80
- Time Saving
- Effective/ efficient

Standardized way to solve the complex problem

If (x + 2) = 1000,
what is $x^2 - 4$ =?

(x + 2) (x - 2) = 1000* 996
= 996,000

Final Thoughts

- Benefits of Standards in Oncology Studies
- Oncology-specific standards
- E2E Standards-driven process

Contact Us!

Contact Clindata Insight to learn more about Oncology.
Youtube in https://www.youtube.com/channel/UCK1H3T0w1S_qOe5bKVh0bYw

Email us at
klee@clindatainsight.com
consulting@clindatainsight.com

Like us on Facebook @ Facebook.com/clindatainsight

Twitter @clindatainsight

WeChat @clindatainsight

Clindata is a CDISC Gold Member