Applying RECIST v1.1 in Oncology Study

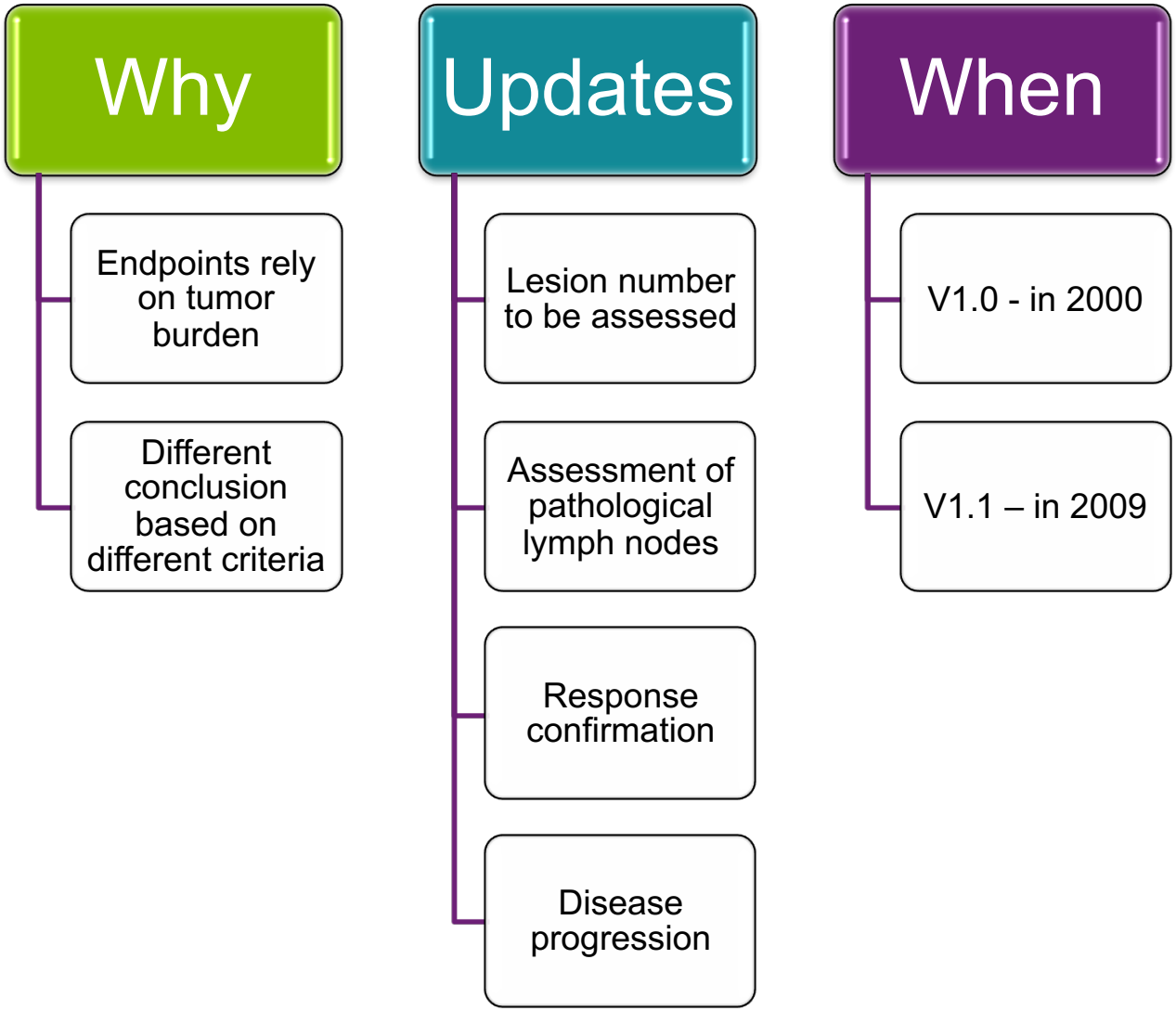
Ni Guan
Biostatistician, QuintilesIMS
MAY 19, 2017

Brief Introduction to RECIST

Key Points for Analysis

Discussion for Confirmation Rule

Brief Introduction to RECIST



Basic Concept

Measurable vs. Non-measurable

- ••Refer to RECIST v1.1 section 3.1.1 and 3.1.2
- ••Basically based on diameters and disease type

Method of assessment

- ••Preferred method: CT and MRI
- ••Refer to RECIST v1.1 section 3.2.

Baseline documentation of target and non-target lesions

- ••Selected based on size, representativeness and reproducibility;
- ••Identified by either investigator or independent committee at baseline.

Basic Concept

- Response

Target Lesion Response criteria

- ••Based on the sum of diameters of all target lesions identified at baseline
- ••Refer to section 4.3.1
  - ••CR – Disappearance of all target lesions (nodal lesion with SDIAM < 10 mm)
  - ••PR – At lease 30% decrease in sim of diameters of target lesions (reference: baseline sum diameters)
  - ••PD – At lease 20% increase in the sum of diameters of target lesions (reference: smallest sum on study) and absolute increase ≥ 5 mm;
  - ••SD – Neither PR nor PD

Non-target Lesion Response Criteria

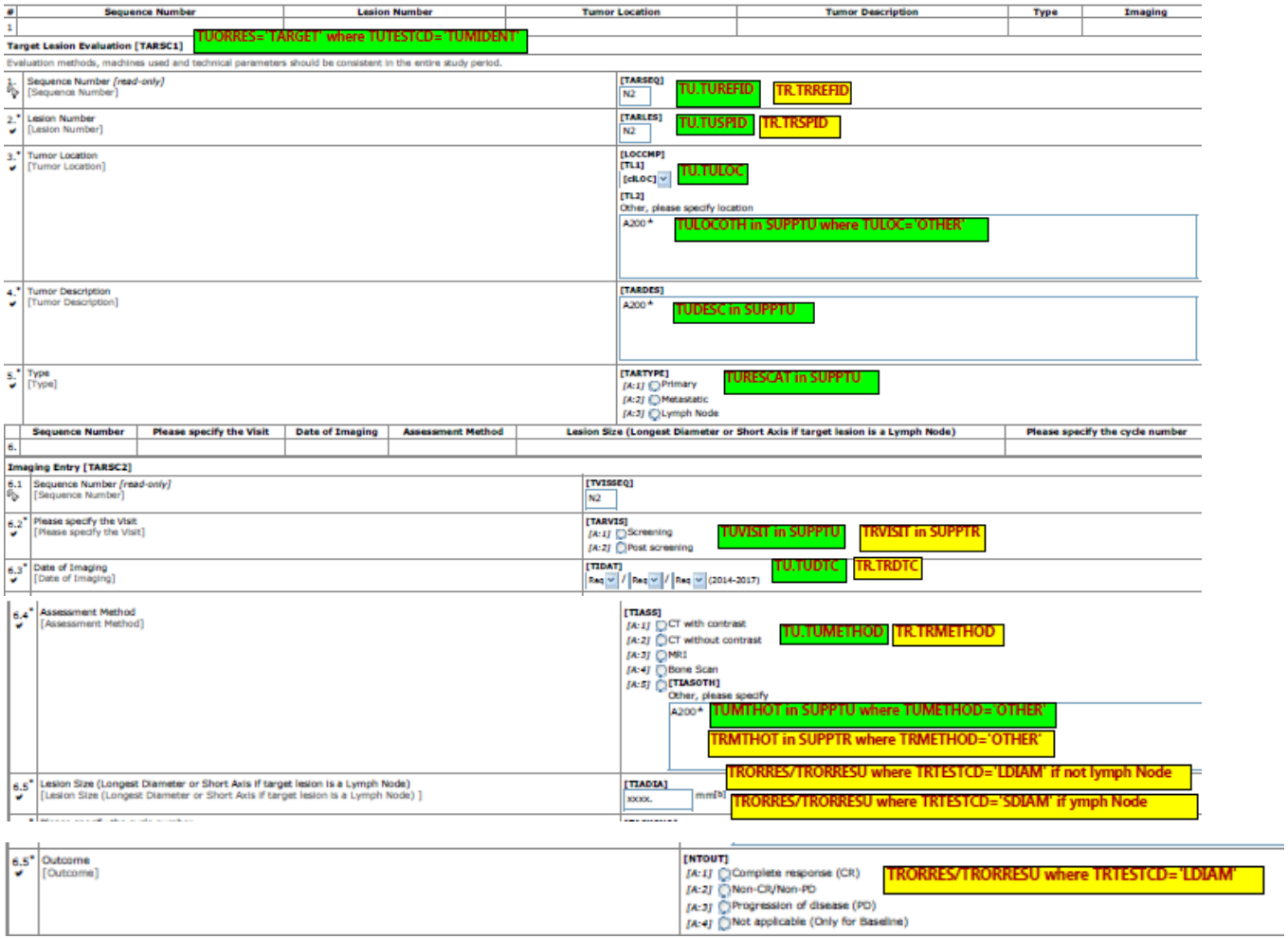
- ••Refer to section 4.3.3
  - ••CR – Same as above
  - ••Non-CR/Non-PD - Persistence of one or more non-target lesion(s) and/or maintenance of tumor marker level above the normal limits.
  - ••PD - Unequivocal progression of existing non-target lesions.

New Lesion

- ••Yes vs. No, refer to section 4.3.5

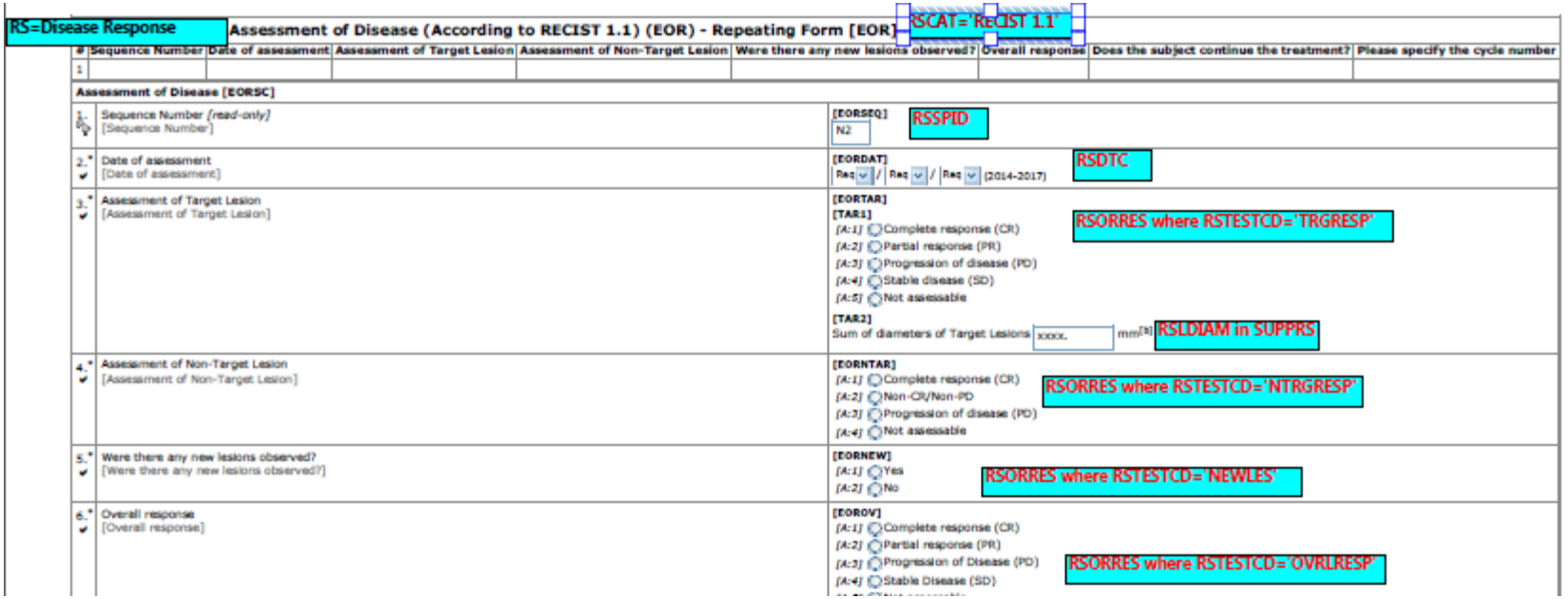
Basic Concept

- Relevant CRF



Basic Concept

- Relevant CRF



Key Points for Analysis

- Before Analysis

Number of lesions	• Total number (≤ 5) • Number per organ (≤ 2) • Number consistent
Diameter (measurable)	• Non-Nodal lesions (LDIAM): ≥ 10 mm by CT • Nodal lesions (SDIAM): ≥ 15 mm by CT
Method for scan	• Consistent with the diameter criteria • Consistent per lesion through-out the study

Total Number of target lesions

- Reduced from 10 to 5
- ≤ 2 per organ
- Organ should be specified in protocol, different for each trial

Diameters

- Non-nodal lesions: Longest diameter ≥ 10 mm
- Nodal lesions: Shortest diameter ≥ 15 mm
- Criteria could be adjusted based on the slice thickness of CT

Method

- Preferred method: CT scan and MRI

Key Points for Analysis

- Response date

SCAN DATE vs. ASSESSMENT DATE

- TU and TR record the scan date, while RS record the assessment date.
- Scan date of different component can be different
- Assessment date can be the same as or after scan date(s), but can before the latest lesion scan date.

How to derive:

- Determine the effective response date per components
- Determine the overall response date based on the overall response and response date per components.

Confirmation of CR and PR

- For PD: earliest components date leading to PD

NEW	NEW1.1	Unequivocal Progression	2016-04-16
NON-TARGET	NT1.1	Non-CR/Non-PD	2016-04-18
NON-TARGET	NT2.2	Non-CR/Non-PD	2016-04-18
TARGET	T1.1	30.7	2016-04-18
TARGET	T2.2	30.7	2016-04-18

New Lesions Observed	Yes	2016-04-22
Non-target Response	Non-CR/Non-PD	2016-04-22
Overall Response	Progression of Disease (PD)	2016-04-22
Target Response	Stable disease (SD)	2016-04-22

TARGET	T1.1	16	2016-07-12
TARGET	T2.2	14	2016-07-12
NON-TARGET	NT1.1	Non-CR/Non-PD	2016-07-13
TARGET	T3.3	23	2016-07-13

New Lesions Observed	No	2016-07-13
Non-target Response	Non-CR/Non-PD	2016-07-13
Overall Response	Progression of Disease (PD)	2016-07-13
Target Response	Progression of disease (PD)	2016-07-13

- For response other than PD – latest component date

NON-TARGET	NT1.1	Non-CR/Non-PD	2016-01-13
NON-TARGET	NT2.2	Non-CR/Non-PD	2016-01-13
NON-TARGET	NT3.3	Non-CR/Non-PD	2016-01-13
TARGET	T1.1	14	2016-01-13
NON-TARGET	NT4.4	Non-CR/Non-PD	2016-01-19

New Lesions Observed	No	2016-01-19
Non-target Response	Non-CR/Non-PD	2016-01-19
Overall Response	Stable Disease (SD)	2016-01-19
Target Response	Stable disease (SD)	2016-01-19

Endpoints

- Best Overall Response

Definition

- Best response recorded from the start of the study treatment until the end of treatment
- Consider subsequent therapy or not;
- Consider confirmation or not;
- Whether SD meet the minimum time from timeline

Confirmation

- Required for non-randomized trial with response of the primary endpoints
- Not required for randomized phase II or phase III trials or studies with SD/PD of the primary endpoint.
- Only CR/PR is required for confirmation.

Endpoints

- BOR and confirmation

- Rule in RECIST

Table 3 – Best overall response when confirmation of CR and PR required.

Overall response First time point	Overall response Subsequent time point	BEST overall response
CR	CR	CR
CR	PR	SD, PD or PR[a]
CR	SD	SD provided minimum criteria for SD duration met, otherwise, PD
CR	PD	SD provided minimum criteria for SD duration met, otherwise, PD
CR	NE	SD provided minimum criteria for SD duration met, otherwise NE
PR	CR	PR
PR	PR	PR
PR	SD	SD
PR	PD	SD provided minimum criteria for SD duration met, otherwise, PD
PR	NE	SD provided minimum criteria for SD duration met, otherwise NE
NE	NE	NE

CR = complete response, PR = partial response, SD = stable disease, PD = progressive disease, and NE = inevaluable.

a If a CR is *truly* met at first time point, then any disease seen at a subsequent time point, even disease meeting PR criteria relative to baseline, makes the disease PD at that point (since disease must have reappeared after CR). Best response would depend on whether minimum duration for SD was met. However, sometimes 'CR' may be claimed when subsequent scans suggest small lesions were likely still present and in fact the patient had PR, not CR at the first time point. Under these circumstances, the original CR should be changed to PR and the best response is PR.

- To reduce bias may need central review.

Endpoints

- PFS

- ADT should take into consideration of
  - › Missing tumor assessment
  - › New anti-cancer therapy

Summary

Amendment in RECIST v1.1

- Lesion number
- PD criteria

Basic concepts in RECIST v1.1

- Measurable vs. Non-measurable
- Target vs. Non-target
- Response criteria

Endpoints

- BOR (Confirmation)
- PFS


Questions?