Supplementary Appendix

Table S1. Inconsistent Primary Outcome Measures (POMs)

Example	Registration Record	Protocol and/or Publication
1	**NCT01605136** [U.S. Trial]— • **POM:.** "**Duration of direct sunlight exposure**" **NCT00979745** [E.U. Trial]— • **POM:.** "Severity of **phototoxic reaction** measured by visual analogue scale"	**Publication**[1]— • **POM**: "**Duration of direct exposure to sunlight**…" • **SOM:** "**Phototoxic reactions**…"
2	**NCT01680744** — "… renal function **[OF DONOR]** as determined by **creatinine and cystatin c between neurological death and organ recovery**"	**Publication**[2] — "The primary outcome, delayed graft function (**the recipient's requirement for dialysis during the first week after transplantation**)…" **Protocol** — "delayed graft function (DGF) **[OF RECIPIENT],** defined as **the need for renal dialysis within the first week post-transplantation.**"

Table S2. Examples of Additional Issues in Reporting POMs

Issue Type 1: Varying Amounts of Detail in Reporting the Specific Measurement for POMs

Level of Specification[3]	**Registration Record (NCT01412541)**	**Protocol**	**Publication**[4]
1 – Domain	[Lesion Status]	[Lesion Status]	[Lesion Status]
2 – Specific Measurement	"Primary Patency"	"Primary Patency is defined as **the absence of target lesion restenosis (defined by DUS peak systolic velocity ratio (PSVR) ≥ 2.5) and freedom from target lesion revascularization (TLR)**."	"The primary effectiveness measure was primary patency of the target lesion at 12 months. Primary patency was defined as **the absence of evidence of binary restenosis, as detected by means of duplex ultrasonography and adjudicated by staff at the ultrasonographic core laboratory, and freedom from target-lesion revascularization, as adjudicated by the clinical-events committee.**"

Level of Specification	**Registration Record (NCT01866319)**	**Protocol**	**Publication**[5]
1 – Domain	"Melanoma"	"**Advanced** Melanoma"	"**Advanced** Melanoma"
2 – Specific Measurement	"Progression-free Survival (PFS)"	"progression-free survival (PFS) … **or death due to any causes, whichever occurs first…**" "…**utilize RECIST 1.1 criteria for response assessment**"	"progression-free survival (defined as the time from randomization to documented disease progression according to **RECIST or death from any cause**)"

Issue Type 2: Problems in Reporting the Time Frame for POMs

Level of Specification	Registration Record (NCT00786474)	Protocol	Publication[6]
1 – Domain	"Embolism"	"Embolism"	"Embolism"
2 – Specific Measurement	"Arterial thromboembolic events, defined as • an ischemic stroke, • transient ischemic attack, or • systemic embolism"	"ATE [Arterial thromboembolic events], defined by one or more of the events listed below: 1) Ischemic stroke…, 2) Transient ischemic attack…, 3) Systemic embolism…"	"arterial thromboembolism, including • stroke (ischemic or hemorrhagic), • transient ischemic attack, and systemic embolism"
Time Frame	"**Measured throughout the study**"	"**followed for at least 36 days … or longer…**"	"**…by 37 days after the procedure**"

Level of Specification	Registration Record (NCT01878799)	Protocol	Publication[7]
1 – Domain	"Hepatitis C / HIV"	"Chronic hepatitis C/HIV"	"chronic hepatitis C virus (HCV) infection/ HIV"
2 – Specific Measurement	"To assess the safety, tolerability and efficacy of a fixed dose combination (FDC) of GS-7977/GS-5885 tablets for **12 weeks**"	"Proportion of patients achieving SVR_{12} [sustained viral response] (HCV RNA <LLOQ 12 weeks after completion of treatment)"	"the proportion of patients with sustained viral response (plasma HCV RNA level <12 IU/mL) 12 weeks after end of treatment."
Time Frame	"**Day 0, Day 1, Day 3, Day 5, Day 7, Day 10,Week 2, Week 3, Week 4, Week 6, Week 8, Week 12, Week 14, Week 16, Week 20, Week 24, Week 36, Week 48, Week 60**"	"**12 weeks after cessation of therapy**"	"**12 weeks after end of treatment**"

Level of Specification	Registration Record (NCT01844505)	Protocol	Publication[8]
1 – Domain	"Unresectable or Metastatic Melanoma"	"Untreated Unresectable or Metastatic Melanoma"	"Untreated Melanoma"
2 – Specific Measurement	"Endpoint of Overall Survival (OS)"	"Overall Survival"	"overall survival"
Time Frame	"**Approximately up to 44.1 months**"	**N/A**	**N/A**

Level of Specification	Registration Record (NCT01866319)	Protocol	Publication[5]
1 – Domain	"Melanoma"	"Advanced Melanoma"	"Advanced Melanoma"
2 – Specific Measurement	"Progression-free Survival (PFS)"	"progression-free survival (PFS) … or death due to any causes, whichever occurs first"	"progression-free survival (defined as the time from randomization to documented disease progression according to RECIST or death from any cause)"
Time Frame	"**Up to 2 years" AND "Up to 30 months**"	**N/A**	**N/A**

Level of Specification	Registration Record (NCT01942135)	Protocol	Publication[9]
1 – Domain	[Oncology]	[Oncology]	[Oncology]
2 – Specific Measurement	Progression-Free Survival	"Progression-Free Survival (PFS) as assessed by the Investigator"	"investigator-assessed progression-free survival according to RECIST, version 1.1."
Time Frame	"**approximately 10 months**"	**N/A**	**N/A**

Level of Specification	Registration Record (NCT01642004)	Protocol	Publication[10]
1 – Domain	[Oncology]	[Oncology]	[Oncology]
2 – Specific Measurement	"Overall Survival (OS)"	"OS is defined as the time from randomization to the date of death"	"overall survival"
Time Frame	"**38 months**"	**N/A**	"**followed for survival continuously while they were receiving the study drugs and then every 3 months after discontinuation of treatment**"

REFERENCES

1. Langendonk JG, Balwani M, Anderson KE, et al. Afamelanotide for Erythropoietic Protoporphyria. The New England journal of medicine 2015;373:48-59.
2. Niemann CU, Feiner J, Swain S, et al. Therapeutic Hypothermia in Deceased Organ Donors and Kidney-Graft Function. The New England journal of medicine 2015;373:405-14.
3. Zarin DA, Tse T, Williams RJ, Califf RM, Ide NC. The ClinicalTrials.gov results database--update and key issues. The New England journal of medicine 2011;364:852-60.
4. Rosenfield K, Jaff MR, White CJ, et al. Trial of a Paclitaxel-Coated Balloon for Femoropopliteal Artery Disease. The New England journal of medicine 2015;373:145-53.
5. Robert C, Schachter J, Long GV, et al. Pembrolizumab versus Ipilimumab in Advanced Melanoma. The New England journal of medicine 2015;372:2521-32.
6. Douketis JD, Spyropoulos AC, Kaatz S, et al. Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation. The New England journal of medicine 2015;373:823-33.
7. Osinusi A, Townsend K, Kohli A, et al. Virologic response following combined ledipasvir and sofosbuvir administration in patients with HCV genotype 1 and HIV co-infection. Jama 2015;313:1232-9.
8. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma. The New England journal of medicine 2015;373:23-34.
9. Turner NC, Ro J, Andre F, et al. Palbociclib in Hormone-Receptor-Positive Advanced Breast Cancer. The New England journal of medicine 2015;373:209-19.
10. Brahmer J, Reckamp KL, Baas P, et al. Nivolumab versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer. The New England journal of medicine 2015;373:123-35.