

The examination is being carried out on the **following application documents**

Description, Pages

1-138 as originally filed

Sequence listings, SEQ ID NO

1-42 as originally filed

Claims, Numbers

1-14 received on 18-10-2018 with letter of 18-10-2018

Drawings, Sheets

1/34-34/34 as originally filed

1 General remarks

- 1.1 With regards to the assessment of novelty and inventive step the documents cited remain those as are numbered in the search report.
- 1.2 The following document is cited by the Examiner. A copy of the document is annexed to the communication and the numbering will be adhered to in the rest of the procedure.

D10 Anonymous: "History of Changes for Study: NCT01024231 - 30.04.2012", 30 April 2012 (2012-04-30), XP055627493,
Retrieved from the Internet: URL:https://clinicaltrials.gov/ct2/history/NCT01024231?V_58=View#StudyPageTop [retrieved on 2019-10-01]

- 1.3 The arguments brought forth by the applicant in his letter dated 18.10.2018 have been carefully considered by the examining division (ED). However, at present, the division does not find said arguments persuasive and hence the requests on file do not meet the requirements of the EPC.

2 **Article 123(2) EPC**

The amendments made to the claims of the present application appear not to contain subject-matter which extends beyond the content of the application as filed. Therefore, the application appears to conform to Article 123(2) EPC.

3 **Article 56 EPC**

- 3.1 Newly introduced document D10 discloses discloses a clinical study in which anti-PD-1 antibody MDX-1106 (BMS-936558, 5C4 and Nivolumab) is administered in combination with anti-CTLA-4 antibody Ipilimumab to patients suffering from stage III or stage IV malignant Melanoma (cf. D10 as a whole).
- 3.2 D10 further discloses experimental cohorts C1-C7 which detail different regimens e.g. C2 detailing the following regimen: an induction dosing schedule solution containing BMS-936558 (1 mg/kg) and Ipilimumab (3 mg/kg) administered intravenously once every three weeks for 9 weeks followed by a maintenance dosing schedule solution containing said antibodies at said doses but administered once every 12 weeks for 48 doses.
- 3.3 D10 also discloses experimental cohort C6 in which anti-PD-1 antibody MDX-1106 (BMS-936558; at 1 mg/kg) is administered to patients intravenously once every 4 weeks and 5 weeks off for 96 weeks.
- 3.4 D10 does not disclose the exact regimen recited in claim 1 but does disclose the recited the exact same antibody combination as well as the dosages used.
- 3.5 Importantly, the application does not demonstrate that a surprising technical effect has been demonstrated with the regimen of claim 1 over those already disclosed in document D1 and thus in view of the closest prior art, the objective technical problem to be solved can be seen as merely the provision of an alternative regimen for the aforementioned antibody combination at said doses.
- 3.6 The above aside, even if an effect were to be demonstrated, in view of the number of different cohorts already tested in document D1 and the sheer number of routine experimentation that is well known to be carried out in clinical trials as can be seen from the history of changes included in document D10, the skilled person would have arrived at the subject-matter of claim 1 without inventive skill and with expectation of success.
- 3.7 Indeed, it is noted that the establishment of dosage regimes is considered a matter of routine for the skilled person (cf. T1979/09).
- 3.8 Therefore, at present inventive step cannot be acknowledged for present claim 1 as well as the claims dependent thereupon.