**Supplementary Table 1: Inclusion and exclusion criteria of the study**

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| --- | --- |
| **Inclusion criteria** | **Exclusion criteria** |
| First diagnosis of histologically proven and unresectable NSCLC with clinical stage IIIa/b | Prior treatment with any other investigational drug within 4 weeks prior to the first dose of the study therapy |
| Completion of RCT (no longer than 1-2 months ago) | Any severe heart disease or any severe concomitant disease (ECOG status >2) |
| Progression-free according to RECIST1.1 criteria at the first assessment after RCT | Patients that show ALK positivity or an activating mutation of the EGFR-TK domain |
| Confirmed presence of mHsp70 on the patient`s tumor, as determined by analysing circulating levels of lipid-bound and free Hsp70 using the lipHsp70 ELISA and defined by elevated exosomal Hsp70 serum levels (above a threshold of 7.4 ng/ml) | NSCLC patients (stage IIIa/b) eligible for initial surgery with a confirmed consent of an Interdisciplinary Tumor Board  Patients with locally advanced or metastatic NSCLC, other than disease with squamous histology |
| Female and male patients, age 18-75 years | Female patients of reproductive potential unwilling to practice a highly effective method of birth control |
| ECOG Status ≤2 | Any serious infection or sepsis |
| Neutrophil count ≥1.5x109/l | Any active autoimmune disease |
| White blood cell count ≥2.5x109/l | Any immunodeficiency syndrome |
| Haemoglobin >10 g/l | Patients with positive HIV test |
| Platelet count ≥100x109/l | Surgery or immunotherapy within 4 weeks before study entry |
| Normal renal function (creatinine <150% ULN) | Patients with known hypersensitivity to any of the administered substances |
| Normal liver function (Bilirubin <200% ULN; G-GT, GPT, GOT <250% ULN) | Radio-, cytostatic-, and immuno-therapy in parallel or within 4 weeks prior to study start |
| Normal blood coagulation (PTT 25-40s) | History of noncompliance with medical regimens |
| Measurable disease according to irRC criteria | Women who are pregnant or breast-feeding |
| Female patients of childbearing potential must have a negative pregnancy test performed during screening period (≤14 days before initiation of study drug dosing). Postmenopausal women must have been amenorrheal for at least 12 months to be considered of non-childbearing potential. Male and female patients of reproductive potential must agree to employ an effective method of birth control throughout the study and for 6 months following discontinuation of the study therapy. | Any disease (including psychotic disorders, drug abuse, active infection, uncontrolled hypertension, unstable angina, congestive heart failure, myocardial infarction within the previous year, serious cardiac arrhythmia requiring medication, hepatic, renal or metabolic disease), metabolic dysfunction, physical examination finding, or clinical laboratory finding likely (in the investigator’s opinion) to affect the evaluation of the study or place the patient at risk whilst on treatment |
| Delivery of a written (signed) Informed Consent document indicating that the patient (or legally acceptable representative) has been informed of all pertinent aspects of the trial prior to enrolment and participation in the study | Receipt of immunosuppressive drugs including high dose systemic corticosteroids within 3 weeks before study entry. Low dose corticosteroids as a common treatment option for patients suffering from chronic obstructive pulmonary disease (COPD) is allowed |
| Ability to comply with study and follow-up procedures | Patients unwilling to, or unable to comply with the protocol |

**Supplementary Table 2: Summary of related Adverse Events (AEs) per group**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Related to study medication | | | | | |
|  | Related | Possibly related | Unlikely | Not related | Not assessable | Total |
| INT | 0 | 3 | 8 | 12 | 0 | 23 |
| CTRL | 2 | 0 | 0 | 13 | 2 | 17 |
| Total | 2 | 3 | 8 | 25 | 2 | 40 |

**Supplementary Table 3: Comparison of the ratios of NK cell subpopulations (responders/non-responders) in the interventional (INT) and control (CTRL) arm at tumor progression**

|  |  |  |
| --- | --- | --- |
| **Tumor progression** | **INT** | **CTRL** |
|  | **responders (n=4)/ non-responders (n=2)** | **responders (n=2)/ non-responders (n=5)** |
| **CD3-/CD16+** | 3.1 (25% vs 8%) | 0.6 (10% vs 18%) |
| **CD3-/CD56+** | 1.8 (18% vs 10%) | 0.3 (5% vs 15%) |
| **CD3-/CD94+** | 1.5 (15% vs 10%) | 0.4 (3% vs 8%) |
| **CD3-/NKG2D+** | 1.7 (19% vs 11%) | 0.2 (3% vs 13%) |
| **CD3-/NKp30+** | 1.3 (13% vs 10%) | 0.3 (4% vs 14%) |
| **CD3-/NKp46+** | 1.25 (15% vs 12%) | 0.3 (4% vs 12%) |
| **CD3-/CD69+** | 3.6 (18% vs 5%) | 1.2 (9% vs 7%) |