| **Arm** | **Cohort** | **N** | **Dose per injection** | **Mode of administration** | **Concentration**  (mg/mL) |
| --- | --- | --- | --- | --- | --- |
| A | 1 | 3 | 2 mg twice daily | The first lesion was treated for 6 weeks (induction treatment; Days 1, 2, 3, 15, 22, 29, and 36). Second and third lesions could be injected sequentially, in Weeks 7 to 12, and then Weeks 13 to 18, respectively. This was followed by a maintenance phase with 1 treatment day every second week in last injected lesion for ≤ 20 weeks. | 20 |
| 2 | 3 | 3 mg twice daily |
| 3 | 3 | 4 mg twice daily |
| 4 | 3 | 4 mg Day 1, then 5 mg |
| 5 | 4 | 4 mg Day 1, then 6 mg |
| 6 | 4 | 4 mg Day 1, then 7 mg |
| 7 | 3 | 4 mg Day 1, then 6 mg | 10 |
| B\* | 1 | 3 | 3 mg per lesion | One injection in multiple lesions on the same dosing days (Days 1, 2, 3, 8, 22), then every 3 weeks for maintenance up to 43 weeks. | 10-20 |
| 2 | 2 | 4 mg per lesion | 20 |
| B\*\* | 1 | 5 | 3 mg per injection | A minimum of 1 lesion was treated with a fixed dose of LTX-315 per injection on Days 1, 2, 8, 9, 15, and 16. The number of injections to each lesion was calculated per lesion based on tumor volume. For practical reasons, a maximum of 12 injections per day was allowed in a minimum of a 1-hour period to 3-12 lesions depending on lesion volume. | 10 |
| 2 | 3 | 4 mg per injection |
| 3 | 3 | 5 mg per injection |

**Supplementary Table 1A.** Dosing schedule per arm and cohort

**Supplementary Table 1B.** Summary of drug-related treatment-emergent adverse events occurring in at least 10% of patients or grade ≥ 3 in patients in Arm A.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Arm A** | | | | | | | | | | | | | |
|  | Cohort 1 | | Cohort 2 | | Cohort 3 | | Cohort 4 | | Cohort 5 | | Cohort 6 | | Cohort 7 | |
|  | Overall | Grade ≥ 3 | Overall | Grade ≥ 3 | Overall | Grade ≥ 3 | Overall | Grade ≥ 3 | Overall | Grade ≥ 3 | Overall | Grade ≥ 3 | Overall | Grade ≥ 3 |
| Hypotension | 1 |  | 3 |  | 4 |  | 2 |  | 2 |  | 2 |  | 1 |  |
| Flushing |  |  |  |  | 1 |  | 3 |  | 1 |  | 1 |  | 2 |  |
| Pruritus |  |  | 1 |  |  |  | 1 |  | 1 |  | 1 |  |  |  |
| Rash |  |  | 1 |  |  |  | 1 |  |  |  |  |  | 1 |  |
| Musculoskeletal and connective tissue disorders |  |  | 1 |  |  |  | 2 |  |  |  | 1 |  |  |  |
| Fatigue |  |  |  |  |  |  | 1 |  | 2 |  | 1 |  |  |  |
| Hypersensitivity |  |  |  |  | 1 |  |  |  | 1 | 1 | 1 |  | 1 |  |
| Injection site paraesthesia |  |  |  |  | 1 |  | 1 |  | 1 |  | 1 |  |  |  |
| Paraesthesia |  |  |  |  |  |  |  |  | 2 |  | 1 |  | 1 |  |
| Anaphylactic reaction |  |  |  |  |  |  | 1 | 1 |  |  | 1 | 1 | 1 | 1 |
| Diarrhoea |  |  | 1 |  |  |  | 1 |  | 1 |  |  |  |  |  |
| Local pain |  |  |  |  |  |  |  |  |  | 1 |  |  |  |  |
| Syncope |  |  |  |  |  |  |  | 1 |  |  |  |  |  |  |
| Sepsis |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 |

**Supplementary Table 1C.** Summary of drug-related treatment-emergent adverse events occurring in at least 10% of patients or grade ≥ 3 in patients in arm B.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Arm B\* | | | | Arm B\*\* | | | | | |
|  | Cohort 1 | | Cohort 2 | | Cohort 1 | | Cohort 2 | | Cohort 3 | |
|  | Overall | Grade ≥ 3 | Overall | Grade ≥ 3 | Overall | Grade ≥ 3 | Overall | Grade ≥ 3 | Overall | Grade ≥ 3 |
| Hypotension |  |  |  |  | 1 |  | 1 | 1 | 1 |  |
| Flushing |  |  |  |  | 2 |  |  |  | 1 |  |
| Pruritus |  |  |  |  | 1 |  | 1 |  |  |  |
| Rash | 1 |  |  |  | 2 |  |  |  |  |  |
| Hypertension |  |  |  |  | 1 | 1 | 1 |  | 1 | 1 |
| Rash maculo papular |  |  |  |  | 1 |  |  |  | 1 |  |
| Local pain |  |  |  |  | 1 |  |  |  | 1 |  |