**Supplementary Table S1. Clinical characteristics of representative patients who developed thyroid dysfunction**

| Case   | Age | Sex | Tumor       | TPOAb (IU/ml) | TgAb (IU/ml) | TRAb (IU/ml) | Onseta (days) | LT4c (µg/day) | Ultrasonography findings                      |
|--------|-----|-----|-------------|---------------|--------------|--------------|---------------|--------------|---------------------------------------------|
| Pem020 | 71  | F   | MM          | 38.9b         | 123.5b       | 449.9b       | 0.3           | 0.3          | 21              | 100 Atrophy, irregular echo pattern          |
| Pem010 | 77  | M   | NSCLC       | 198.6b        | 600b         | 343.2        | 0.3           | 0.6          | 68              | 75 Atrophy, irregular echo pattern          |
| Pem037 | 70  | F   | NSCLC       | 176.1b        | 259.4b       | 10           | 0.5           | 2.3b         | 166 Not required Enlargement, irregular echo pattern |

Normal ranges: TPOAb < 16 IU/ml, TgAb < 28 IU/ml, TRAb < 2.0 IU/ml. Abbreviations: TPOAb, anti-thyroid peroxidase antibodies; TgAb, anti-thyroglobulin antibodies; TRAb, anti-thyrotrophin receptor antibodies; LT4, levothyroxine; MM, malignant melanoma; NSCLC, non-small cell lung carcinoma. aDays to onset of destructive thyroiditis from the first pembrolizumab treatment. bTiter above the upper normal range. cThe dose of replacement levothyroxine
### Supplementary table 2. Characteristics of the patients who were treated with pembrolizumab and evaluated by thyroid ultrasonography

|                        | Total | (-) | (+) |   |   |
|------------------------|-------|-----|-----|---|---|
| MM                     | 5     | 4   | 1   |   |   |
| NSCLC                  | 10    | 5   | 5   |   |   |
| UC                     | 1     | 1   | 0   |   |   |
| Tumor type             |       |     |     | 0.346 |   |
| Male                   | 9     | 7   | 2   |   |   |
| Female                 | 7     | 3   | 4   |   |   |
| Sex                    |       |     |     | 0.302 |   |
| Age, years (range)     | 70 ± 6 | 69 ± 7 | 71 ± 5 |   | 0.609 |
|                        | (58–80) | (58–80) | (63–77) |   |   |
| Follow-up period (days)| 430 ± 227 | 347 ± 197 | 568 ± 220 |   | 0.056 |

| p value                |   |
|------------------------|---|
| (-)                    |   |
| (+)                    |   |

| Abbreviations: MM, malignant melanoma; NSCLC, non-small cell lung carcinoma; UC, urothelial cell carcinoma. |
Supplementary table 3. Characteristics of the patients who were treated with nivolumab and evaluated by thyroid ultrasonography

| Tumor type | Total | Irregular echo pattern | $p$ value |
|------------|-------|------------------------|-----------|
|            | (n = 26) | (n = 9) | (n = 17) | |
| MM         | 3     | 2         | 1         | |
| NSCLC      | 8     | 2         | 6         | |
| RCC        | 3     | 1         | 2         | 0.302 |
| HN         | 7     | 3         | 4         | |
| GC         | 5     | 1         | 4         | |
| Male       | 16    | 4         | 12        | 0.234 |
| Female     | 10    | 5         | 5         | |
| Age, years | $62 \pm 13$ | $62 \pm 8$ | $62 \pm 15$ | 0.875 |
| (range)    | (28–70) | (49–70) | (28–78) |
| Follow-up period | $326 \pm 224$ | $317 \pm 188$ | $331 \pm 247$ | 0.887 |

**Abbreviations:** MM, malignant melanoma; NSCLC, non-small cell lung carcinoma; RCC,
renal cell carcinoma; HN, head and neck cancer; GC, gastric cancer.
Supplementary Figure legends

Supplementary Figure S1. Clinical features of thyroid dysfunction in patients treated with pembrolizumab

Changes in FT3, FT4, and TSH levels over 240 days in a patient who developed destructive thyroiditis (Pem020) (A–C) or hypothyroidism (Pem010) (D–F). Gray areas indicate the normal range of each value. Arrows indicate the day of starting levothyroxine replacement treatment.

FT3, serum free triiodothyronine; FT4, serum free thyroxine; TSH, serum thyroid stimulating hormone; (d), day.

Supplementary Figure S2. Clinical features of hyperthyroidism in the patient treated with pembrolizumab

Changes in FT3, FT4, and TSH levels over 240 days in the patient who developed hyperthyroidism (Pem037) (A–C). Gray areas indicate the normal range of each value. A representative image showing the increased level of $^{99m}$Tc pertechnetate uptake in the thyroid at the time of thyrotoxicosis diagnosis (D). FT3, serum free triiodothyronine; FT4, serum free thyroxine; TSH, serum thyroid stimulating hormone; (d), day.