**SUPPLEMENT**

**SUPPLEMENTARY TABLES**

**Supplementary Table 1. Serious Adverse Events**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **n (%)** | **0.3→10 mg/kg**  **(n=3)** | **1 mg/kg**  **(n=3)** | **3 mg/kg**  **(n=3)** | **10 mg/kg**  **(n=3)** | **20 mg/kg**  **(n=7)** | **Total**  **(n=19)** |
| **Patients with any serious adverse event** | **2 (66.7)** | **2 (66.7)** | **1 (33.3)** | **1 (33.3)** | **5 (71.4)** | **11 (57.9)** |
| Abdominal pain |  | 1 (33.3) |  |  | 1 (14.3) | 2 (10.5) |
| Anemia |  |  | 1 (33.3) |  | 2 (28.6) | 3 (15.8) |
| Bullous pemphigoid |  |  | 1 (33.3) |  |  | 1 (5.3) |
| Cerebrovascular accident |  |  |  |  | 1 (14.3) | 1 (5.3) |
| Colitis |  |  |  |  | 1 (14.3) | 1 (5.3) |
| Cystitis  noninfective | 1 (33.3) |  |  |  |  | 1 (5.3) |
| Dehydration |  | 1 (33.3) |  |  |  | 1 (5.3) |
| Diarrhea |  | 1 (33.3) |  |  | 1 (14.3) | 2 (10.5) |
| Dyspnea |  |  |  |  | 1 (14.3) | 1 (5.3) |
| Embolism | 1 (33.3) |  |  |  |  | 1 (5.3) |
| Fever |  |  |  |  | 1 (14.3) | 1 (5.3) |
| Gastroparesis |  |  |  | 1 (33.3) |  | 1 (5.3) |
| Hypokalemia |  |  |  | 1 (33.3) | 1 (14.3) | 2 (10.5) |
| Keratoacanthoma |  |  |  |  | 1 (14.3) | 1 (5.3) |
| Localized edema |  | 1 (33.3) |  |  | 1 (14.3) | 2 (10.5) |
| Nausea |  | 1 (33.3) |  | 1 (33.3) | 1 (14.3) | 3 (15.8) |
| Rectal hemorrhage |  |  |  |  | 1 (14.3) | 1 (5.3) |
| Skin infection |  |  | 1 (33.3) |  |  | 1 (5.3) |
| Soft tissue infection |  | 1 (33.3) |  |  |  | 1 (5.3) |
| Vomiting |  | 1 (33.3) |  | 1 (33.3) | 1 (14.3) | 3 (15.8) |

**Supplementary Table 2. Treatment-Related Serious Adverse Events**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **n (%)** | **0.3→10 mg/kg**  **(n=3)** | **1 mg/kg**  **(n=3)** | **3 mg/kg**  **(n=3)** | **10 mg/kg**  **(n=3)** | **20 mg/kg**  **(n=7)** | **Total**  **(n=19)** |
| **Patients with any treatment-related serious adverse event** |  |  | **1 (33.3)** | **1 (33.3)** | **3 (42.9)** | **5 (26.3)** |
| Anemia |  |  |  |  | 1 (14.3) | 1 (5.3) |
| Bullous pemphigoid |  |  | 1 (33.3) |  |  | 1 (5.3) |
| Colitis |  |  |  |  | 1 (14.3) | 1 (5.3) |
| Dyspnea |  |  |  |  | 1 (14.3) | 1 (5.3) |
| Gastroparesis |  |  |  | 1 (33.3) |  | 1 (5.3) |
| Hypokalemia |  |  |  | 1 (33.3) |  | 1 (5.3) |
| Keratoacanthoma |  |  |  |  | 1 (14.3) | 1 (5.3) |
| Nausea |  |  |  | 1 (33.3) |  | 1 (5.3) |
| Skin infection |  |  | 1 (33.3) |  |  | 1 (5.3) |
| Vomiting |  |  |  | 1 (33.3) |  | 1 (5.3) |

**Supplementary Table 3. Treatment-Related Adverse Events Occurring During the Dose-Limiting Toxicity Assessment Windowa**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **0.3→10 mg/kg**  **(n=3)** | | **1 mg/kg**  **(n=3)** | | **3 mg/kg**  **(n=3)** | | **10 mg/kg**  **(n=3)** | | **20 mg/kg**  **(n=7)** | | **Total**  **(n=19)** | |
| **n (%)** | **Any Grade** | **Grade**  **≥3b** | **Any Grade** | **Grade**  **≥3b** | **Any Grade** | **Grade**  **≥3b** | **Any Grade** | **Grade**  **≥3b** | **Any Grade** | **Grade**  **≥3b** | **Any Grade** | **Grade**  **≥3b** |
| **Patients with any event** | **1**  **(33.3)** | **0**  **(0.0)** | **0**  **(0.0)** | **0**  **(0.0)** | **0**  **(0.0)** | **0**  **(0.0)** | **0**  **(0.0)** | **0**  **(0.0)** | **3 (42.9)** | **2 (28.6)** | **4**  **(21.1)** | **2**  **(10.5)** |
| Anemia |  |  |  |  |  |  |  |  | 1 (14.3) | 1 (14.3) | 1 (5.3) | 1 (5.3) |
| Hyperthyroidism | 1 (33.3) |  |  |  |  |  |  |  | 1 (14.3) |  | 2 (10.5) |  |
| Lipase increase |  |  |  |  |  |  |  |  | 1 (14.3) | 1 (14.3) | 1 (5.3) | 1 (5.3) |

a Defined as the first 21 days of treatment.

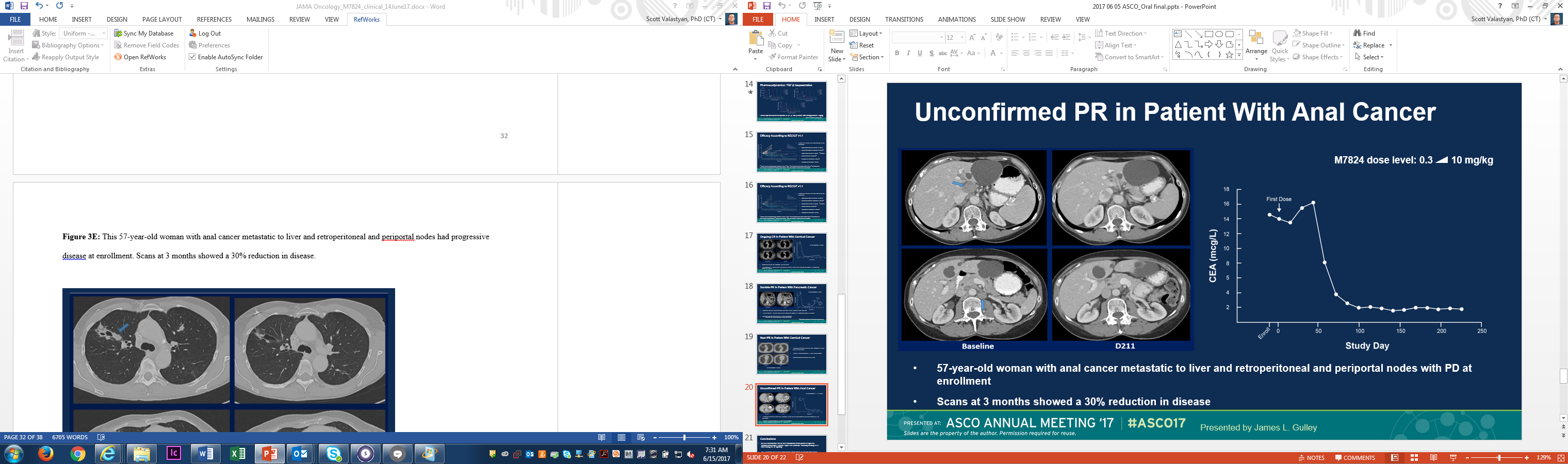
b Both treatment-related grade ≥3 events (anemia and lipase increased) were grade 3.

**Supplementary Table 4: All Adverse Events That Were Either Grade ≥3 or Occurred in >1 Patient**

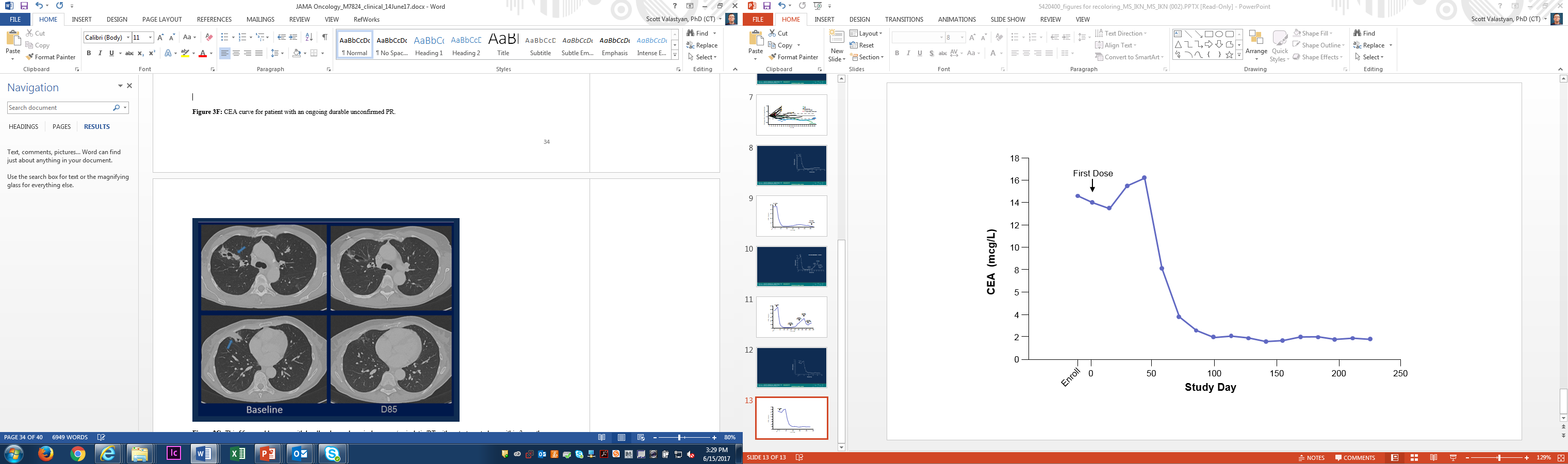
|  |  |  |  |
| --- | --- | --- | --- |
| **n (%)** | | **All Adverse Events** | |
|
| Any Grade | Grade ≥3 |
| **Patients with any event** | | **19 (100.0)** | **12 (63.2)** |
| **Blood and lymphatic system disorders** | | **6 (31.6)** | **4 (21.1)** |
|  | Anemia | 6 (31.6) | 4 (21.1) |
| **Endocrine disorders**  Hyperthyroidism | | **4 (21.1)**  2 (10.5) | **0**  0 |
|  | Hypothyroidism | 3 (15.8) | 0 |
| **Gastrointestinal disorders** | | **15 (78.9)** | **5 (26.3)** |
|  | Abdominal pain | 4 (21.1) | 2 (10.5) |
|  | Abdominal pain upper | 2 (10.5) | 0 |
|  | Colitis | 1 (5.3) | 1 (5.3) |
|  | Constipation | 4 (21.1) | 0 |
|  | Diarrhea  Gastroparesis | 3 (15.8)  1 (5.3) | 1 (5.3)  1 (5.3) |
|  | Large intestinal hemorrhage | 2 (10.5) | 0 |
|  | Mouth hemorrhage | 2 (10.5) | 0 |
|  | Nausea | 9 (47.4) | 3 (15.8) |
|  | Rectal hemorrhage | 1 (5.3) | 1 (5.3) |
|  | Vomiting | 8 (42.1) | 2 (10.5) |
| **General disorders and administration site conditions** | | **11 (57.9)** | **0 (0.0)** |
|  | Fatigue  Influenza-like illness | 8 (42.1)  3 (15.8) | 0  0 |
|  | Localized edema | 4 (21.1) | 0 |
|  | Noncardiac chest pain | 2 (10.5) | 0 |
|  | Pyrexia | 4 (21.1) | 0 |
| **Infections and infestations** | | **6 (31.6)** | **2 (10.5)** |
|  | Lung infection | 1 (5.3) | 1 (5.3) |
|  | Skin infection | 2 (10.5) | 1 (5.3) |
|  | Soft tissue infection | 1 (5.3) | 1 (5.3) |
| **Investigations** | | **8 (42.1)** | **4 (21.1)** |
|  | Activated partial thromboplastin time prolonged | 2 (10.5) | 1 (5.3) |
|  | Blood creatinine increase | 4 (21.1) | 0 |
|  | Lipase increase  Lymphocyte count decrease  Weight decrease | 1 (5.3)  2 (10.5)  2 (10.5) | 1 (5.3)  2 (10.5)  0 |
| **Metabolism and nutrition disorders** | | **7 (36.8)** | **3 (15.8)** |
|  | Acidosis | 1 (5.3) | 1 (5.3) |
|  | Decreased appetite | 4 (21.1) | 0 |
|  | Dehydration | 1 (5.3) | 1 (5.3) |
|  | Hypokalemia  Hypophosphatemia | 2 (10.5)  2 (10.5) | 2 (10.5)  0 |
| **Musculoskeletal and connective tissue disorders** | | **4 (21.1)** | **1 (5.3)** |
|  | Back pain | 1 (5.3) | 1 (5.3) |
| **Neoplasms benign, malignant and unspecified**  Keratoacanthoma | | **2 (10.5)**  2 (10.5) | **0**  0 |
| **Nervous system disorders** | | **4 (21.1)** | **1 (5.3)** |
|  | Cerebrovascular accident  Peripheral motor neuropathy | 1 (5.3)  2 (10.5) | 1 (5.3)  0 |
| **Renal and urinary disorders** | | **3 (15.8)** | **0** |
|  | Proteinuria | 2 (10.5) | 0 |
| **Reproductive system and breast disorders**  Vaginal hemorrhage | | **2 (10.5)**  2 (10.5) | **0**  0 |
| **Skin and subcutaneous tissue disorders** | | **8 (42.1)** | **0** |
|  | Dermatitis acneiform  Dry skin | 2 (10.5)  2 (10.5) | 0  0 |
|  | Rash maculopapular | 4 (21.1) | 0 |
| **Vascular disorders**  Embolism  Hypertension | | **3 (15.8)**  1 (5.3)  2 (10.5) | **2 (10.5)**  1 (5.3)  1 (5.3) |

**SUPPLEMENTARY FIGURES**

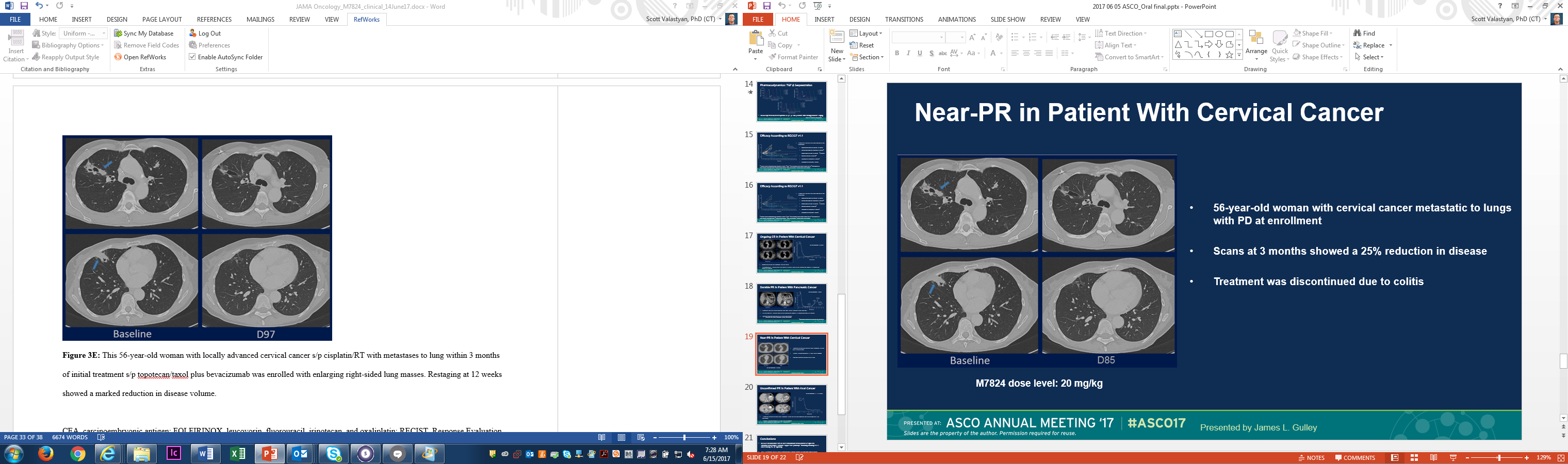
**Supplementary Figure 1A:** This 57-year-old woman with anal cancer metastatic to liver and retroperitoneal and periportal nodes had progressive disease at enrollment. Restaging scans at 3 months showed a PR, which was confirmed at 4.5 months.



**Supplementary Figure 1B:** CEA curve for patient with anal cancer with an ongoing durable confirmed PR.



**Supplementary Figure 1C:** This 56-year-old woman with locally advanced cervical cancer s/p cisplatin/RT with metastases to lung within 3 months of initial treatment s/p topotecan/taxol plus bevacizumab was enrolled with enlarging right-sided lung masses. Restaging at 12 weeks showed a marked reduction in disease volume.



CEA, carcinoembryonic antigen; RT, radiotherapy.