Tumor Lysis Syndrome in Patients With Solid Tumors: A Systematic Review of Reported Cases

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Abstract

Tumor lysis syndrome (TLS) in patients with solid tumors is a rare and potentially fatal condition associated with anti-cancer treatment. Its outcome depends on awareness, identification of high-risk patients, and implementation of appropriate preventive measures. A systematic review was conducted according to PRISMA guidelines of case reports describing the occurrence of TLS in patients with solid tumors, primarily to identify potentially unrecognized or unusual clinical findings and outcomes. We searched the PubMed, EMBASE, and Cochrane databases and conference abstracts and performed manual searches for case reports and case series published in English and describing patients who developed TLS.

A total of 124 studies (118 case reports and six case series) describing the findings for 132 patients were included. The most common cancers were hepatocellular carcinoma (17%, n = 22), lung cancer (13%, n = 17), and melanoma (10%, n = 15). The most common risk factor was metastatic disease (75%, n = 100). TLS was induced by chemotherapy in 48% (n = 64) of the patients. Clinical manifestations of TLS developed within three days of anti-cancer treatment in 37% of the patients (n = 49), while 52% (n = 68) received the full dose of anti-cancer treatment. Gastrointestinal symptoms occurred in 33% of the patients (n = 44), hyperuricemia in 95% (n = 125), and elevated creatinine level occurred in 85% of the patients (n = 112), while 58% (n = 77) of the patients received intravenous fluids, only 49% received allopurinol, and 24% (n = 32) received rasburicase. A total of 101 patients (77%) were treated in the ward, and 54% (n = 71) died. The mortality rate associated with TLS in patients with solid tumors remains high. Adequate management requires awareness, early recognition, and identification of patients at high risk. Interdisciplinary team management is essential to reduce mortality.

Introduction And Background

Tumor lysis syndrome (TLS) is an oncological emergency that occurs secondary to the breakdown of intracellular components such as potassium, phosphorus, and nucleic acids [1]. The release of these products into the bloodstream leads to hyperkalemia, hyperphosphatemia, hyperuricemia, and hypocalcemia, inducing severe complications such as acute renal failure, cardiac arrhythmia, heart failure, seizure, and ultimately death if the patient is not managed appropriately [2,3]. Although the rapid destruction of malignant cells occurs after exposure to anti-cancer treatments such as chemotherapy, radiotherapy, monoclonal antibody treatment, radiofrequency ablation (RFA), corticosteroid treatment, hormonal therapy, and surgery, it can also occur in the absence of anti-cancer treatments, especially if the tumor is bulky or rapidly proliferating. These cases are categorized as spontaneous TLS [4-6].

TLS is commonly observed in hematological malignancies such as Burkitt or non-Burkitt lymphoma and acute leukemia. However, since solid tumors have a relatively prolonged doubling time and slower growth rate, and the effect of therapy takes longer time than hematological malignancies, TLS is rarely observed in solid tumors. However, some cases of TLS have been reported in patients with small-cell lung cancer, breast cancer, melanoma, and sarcoma [7-13]. The risk factors for TLS could be due to patient-related factors such as dehydration, chronic renal failure, elevated pretreatment lactate dehydrogenase (LDH) or uric acid levels, and azotemia or tumor-related factors such as bulkiness, rapid growth, or a tendency to spread to other organs, specifically the bone marrow [14]. TLS is an oncological emergency that needs to be recognized urgently, and if treated early, complications can be prevented, thereby improving the outcomes [15]. The Cairo-Bishop laboratory and clinical criteria are used to diagnose TLS (Table 1) [16]. The presence of two or more laboratory abnormalities starting either three days before or seven days after treatment of the tumor can be used to define laboratory TLS. However, clinical TLS is characterized by the appearance of two laboratory abnormalities and one or more clinical symptoms [17,18].

How to cite this article

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Laboratory criteria
(≥2 of the following): Uric acid ≥ 476 μmol/mL (8 mg/dL) or 25% increase from baseline; Phosphorus ≥ 1.45 mmol/L (4.5 mg/dL) or 25% increase from baseline; Potassium ≥ 6.0 mmol/L (6 mEq/L) or 25% increase from baseline; Calcium ≤ 1·75 mmol/L or 25% decrease from baseline

Clinical criteria
Any of following with laboratory criteria: Creatinine ≥ 1.5 upper limit of normal. Cardiac arrhythmia or sudden death. Seizures.

TABLE 1: Cairo-Bishop criteria for tumor lysis syndrome

TLS is a potentially fatal condition in patients with solid tumors and is associated with worse outcomes if it occurs spontaneously [16]. It has a poor prognosis, especially if it is not diagnosed early; therefore, awareness, recognition, prevention, and early intervention are warranted to prevent the fatal consequences of TLS.

In this paper, we present a systematic review of the reported cases of TLS in patients with solid tumors that developed spontaneously or as adverse effects of anti-cancer treatments such as chemotherapy, immunotherapy, targeted therapy, and hormonal therapy. By describing the occurrence of TLS in patients with solid tumors, we primarily aim to identify potentially unrecognized or unusual clinical findings and outcomes. Also, determine the most common clinical manifestations, time to TLS, number of doses administered before TLS, treatment dosage used, presenting symptoms, and laboratory abnormalities. We also reported the management and clinical outcomes to identify patterns that could facilitate early diagnosis and management of this potentially fatal condition.

Review

Materials and methods

Search Method

Digital databases were used including PubMed, EMBASE, and Cochrane from 1983 to July 1, 2020, for case reports and case series of TLS in patients with solid tumors. In addition, abstracts and presentations from relevant conference proceedings, including the American Society of Clinical Oncology (ASCO) and the European Society for Medical Oncology (ESMO) have been used.

Study Selection and Eligibility criteria

Two independent reviewers (ZA and HT) initially screened the abstracts and titles. Then, two other reviewers (AA and RA) assessed the full texts of the retrieved articles and resolved disagreements in conjunction with a third reviewer (HT). The eligibility criteria were as follows: case reports published in English, describing adults with solid tumors, and reporting spontaneous TLS or TLS that developed after anti-cancer treatments such as chemotherapy, targeted therapy, hormonal therapy, immunotherapy, or radiotherapy. We excluded studies involving hematological tumors, pediatric patients, and non-case reports/series. Keywords for the literature search included published case reports, case series, TLS, solid tumors, and anti-cancer treatment. The search strategy is provided in Appendix 1.

Data Extraction

This study was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [19]. A protocol was created in advance, and data extraction for reported cases of spontaneous TLS or TLS that developed as an adverse effect of anti-cancer treatment was performed independently by two reviewers (ZA and AA), with disagreements resolved by a third reviewer (RA).

We extracted data on patient characteristics (first author, year of publication, age, sex, type of cancer), risk factors (metastasis, elevated pre-treatment LDH level, bulky tumor, and pre-existing renal compromise), and comorbidities. The anti-cancer treatments administered in the cases included chemotherapy, immunotherapy, targeted therapy, hormonal therapy, and radiotherapy. The most common clinical parameters were time to TLS (1-2 days, ≥3 days, spontaneous), number of doses administered before TLS (1 dose, 2-5 doses, >5 doses, spontaneous), dosage of treatment used (full or reduced dose), presenting symptoms, and laboratory abnormalities (uric acid, phosphorus, potassium, calcium, creatinine, urea, and LDH levels). Lastly, we collected information regarding management and clinical outcomes, use of anti-TLS measures, location of treatment received (ward or ICU), and outcome (dead or alive).

Quality Assessment

We assessed the quality of each study by using the criteria recommended by the International Society for Pharmacoepidemiology (ISPE) and the International Society of Pharmacovigilance [20]. Two independent reviewers (HT and RA) assessed the quality of the included studies across the following domains: (i) relevance of the title for TLS, (ii) adequate description of clinical characteristics (demographics, medical
history, physical examination, and outcomes (alive or dead)), (iii) adequate description of anti-cancer drugs (identification of the drug class, dosage, drug reaction, and concomitant therapy) and time to develop adverse events; (iv) adequate description of the adverse event (TLS); and (v) discussion section supporting the relationship between the anti-cancer drug and the reported adverse events (TLS). Each aspect was classified as yes, partial, or no. Any disagreements were resolved by a third reviewer. The results of the assessment are presented in Appendix 2.

Data Synthesis and Analysis

All data were analyzed using IBM SPSS Statistics for Windows, Version 25.0 (Released 2017; IBM Corp., Armonk, New York, United States). Descriptive statistics (mean, percentage, and standard deviation) were used to report continuous variables, and frequencies and percentages were used to present categorical variables.

Results

Study Characteristics

In total, 238 citations were retrieved. After the removal of duplicates, we identified 172 relevant citations and reviewed the full publications. We excluded 17 studies since they were not case reports. We included 124 studies reporting on 132 patients as provided in Figure 1. The characteristics of the included studies are given in Appendix 3.

Quality Appraisal

The quality of the included studies was moderate to high since all included studies had relevant titles,
adequate descriptions of patients’ demographic data (96.7%), current health status (95.1%), medical history (87.9%), physical examination findings (97.5%), and disposition (98%). The anti-cancer drugs were identified for all reported cases of drug-induced TLS, but the drug dosage was not provided in approximately one-quarter of the cases. The duration of drug administration, route, and first dose were reported (70.9%). Furthermore, concomitant therapy had no potential influence (94.3%). A description of the adverse event and severity was reported (92.7%), and an appropriate discussion supporting a causal link between the drug and the adverse events was provided (92.7%).

Patient Characteristics

The median age was 58 years (Interquartile range (IQR) 19-94 years) and the proportion of males was 62% (n = 83). The most common tumors were hepatocellular carcinomas (17%, n = 22), lung cancer (13%, n = 17), melanoma (10%, n = 13), breast cancer (10%, n = 13), prostate cancer (8%, n = 10), and colon cancer (8%, n = 11). The risk factors were metastatic disease in 75% of the patients (n = 100), elevated pre-treatment LDH level in 26% (n = 35), and bulky tumors in 25% (n = 33). The main comorbidities were hypertension, hepatitis B, and diabetes mellitus in 11%, 8%, and 6% of patients, respectively (Table 2).

| Patient characteristics | N (%) |
|-------------------------|-------|
| Median age              | 58, (range 19-94) years |
| Sex                     |       |
| Male                    | 83 (62%) |
| Female                  | 49 (37%) |
| Cancers                 |       |
| HCC                     | 22 (17%) |
| Lung cancer             | 17 (13%) |
| Melanoma                | 13 (10%) |
| Breast cancer           | 13 (10%) |
| Colon cancer            | 11 (8%) |
| Prostatic cancer        | 10 (8%) |
| Renal cell carcinoma    | 6 (5%) |
| Gastric cancer          | 6 (5%) |
| Ovarian cancer          | 5 (4%) |
| Uterine cancer          | 5 (4%) |
| Germ cell tumors        | 3 (2%) |
| Othera                  | 21 (16%) |
| Risk factors            |       |
| Metastasis              | 100 (75%) |
| Elevated pre-treatment LDH | 35 (26%) |
| Bulky tumor             | 33 (25%) |
| Large tumor burden      | 14 (11%) |
| Pre-existing renal compromise | 2 (2%) |
| NA                      | 21 (16%) |
| Main Comorbidities      |       |
| HTN                     | 14 (11%) |
| Hepatitis B             | 10 (8%) |
| DM                      | 8 (6%) |
| Dyslipidemia            | 4 (3%) |
| COPD                    | 3 (2%) |
TABLE 2: Characteristics of patients in the reported cases

| Condition                         | N (%) |
|----------------------------------|-------|
| CKD                              | 3 (2%)|
| Coronary artery disease          | 3 (2%)|
| Other\(^A^\)                     | 6 (5%)|
| NA                               | 94 (71%)|

\(^A^\) Other tumors included choriocarcinoma, osteosarcoma, oligodendroglioma, neuroendocrine tumors, Merkel cell carcinoma, vulvar tumor, gastrointestinal stromal tumors, pheochromocytoma, thymoma, and retroperitoneal soft tissue sarcoma.

\(^B^\) Other comorbidities included congestive heart failure, cirrhosis, and arthritis

**Anti-Cancer Treatment Characteristics**

The most common anticancer treatments that induced TLS were chemotherapy (48%; n = 64), targeted therapy (8%; n = 11), and radiotherapy (7%; n = 9). Details of the classes and names are displayed in Table 3.

### Anti-cancer therapy

| Treatment                                                                 | N (%)  |
|--------------------------------------------------------------------------|--------|
| **Chemotherapy**                                                          |        |
| Alkylating agents (cisplatin, cyclophosphamide, carboplatin, dacarbazine, oxaliplatin, ifosfamide) | 64 (48%) |
| Plant alkaloids (paclitaxel, vincristine, docetaxel, vinblastine, hydroxycamptothecin) |        |
| Anthracyclines (doxorubicin, epirubicin, Adriamycin, mitoxantrone)       |        |
| Topoisomerase inhibitors (etoposide, irinotecan)                         |        |
| Antibiotics (bleomycin, actinomycin, mitomycin)                         |        |
| **Targeted therapy**                                                     |        |
| Kinase inhibitor (paclizabine, sorafenib, sunitinib, imatinib)           | 11 (8%)|
| Anti-Her2 (trastuzumab, pertuzumab)                                      |        |
| Anti-EGFR (cetuximab)                                                   |        |
| Anti-VEGF (bevacizumab)                                                 |        |
| **Radiotherapy**                                                         |        |
| Radiotherapy                                                             | 9 (7%) |
| **Immunotherapy**                                                        |        |
| Interleukin-2 Anti CTLA4 (ipilimumab)                                    | 4 (3%) |
| Autologous lymphocyte therapy                                           |        |
| **Hormonal therapy**                                                     |        |
| Anti ER/PR receptors (letrozole)                                        | 3 (2%) |
| Anti-androgens (bicalutamide)                                           |        |
| Antiestrogen (tamoxifen)                                                |        |
| Combined androgen blockade (goserelin acetate)                           |        |
| Others\(^A^\)                                                            | 7 (5%) |

**Table 3: Characteristics of the anti-cancer treatments**

| Treatment                                                                 | N (%)  |
|--------------------------------------------------------------------------|--------|
| Her2: human epidermal growth factor receptor 2; eGFR: epidermal growth factor receptor; VEGF: vascular endothelial growth factor; CTLA4: cytotoxic T-lymphocyte-associated protein 4; ER: estrogen receptor; PR: progesterone receptor. |        |
| Due to the use of combination therapies such as chemo-targeted, immune-targeted, and chemo-radiation, some variables may not add up to 100%. |        |

\(^A^\) Others included corticosteroid, eribulin, immunomodulatory therapy (thalidomide), bone-modifying agent (zoledronic acid), and surgery.

**Clinical Manifestations of TLS in Patients with Solid Tumors**

TLS occurred spontaneously in 24% (n = 32) of the cases and was treatment-induced in the remaining 76% (n = 100). The number of doses before TLS development was variable, with 17% of the cases showing TLS occurrence after the first dose (n = 23). Time to TLS development was within 5 days of anti-cancer treatment in 37% (n = 49) of the cases, while 52% (n = 68) of the patients received a full dose of anti-cancer treatment. The most commonly reported symptoms were gastrointestinal, genitourinary, and central nervous system symptoms in 33%, 35%, and 26%, respectively. The most reported laboratory abnormalities were hyperuricemia in 95% of the cases (n = 125), followed by elevated creatinine levels in 85% (n = 112) and hyperphosphatemia in 83% (n = 110) of the cases (Table 4).
### TABLE 4: Clinical manifestations of TLS in patients with solid tumors

TLS: tumor lysis syndrome; GI: gastrointestinal; CNS: central nervous system; GU: genitourinary; NA: not available

| TLS manifestation | N (%) |
|-------------------|-------|
| Spontaneous       | 32 (24%) |
| Treatment-induced | 100 (76%) |
| Number of doses before TLS | |
| 1                 | 23 (17%) |
| 2-3 or more       | 5 (4%) |
| NA                | 72 (55%) |
| Time to TLS development | |
| Spontaneous       | 32 (24%) |
| 1-2 days          | 37 (28%) |
| ≥3 days           | 49 (37%) |
| NA                | 13 (10%) |
| Dose of anti-cancer treatment | |
| Spontaneous       | 32 (24%) |
| Full-dose         | 68 (52%) |
| Dose reduction    | 3 (2%) |
| NA                | 29 (22%) |
| Presenting symptoms | |
| GI symptoms       | 44 (33%) |
| GU symptoms       | 44 (33%) |
| CNS symptoms      | 34 (26%) |
| Respiratory symptoms | 25 (19%) |
| Constitutional symptoms | 15 (11%) |
| Others            | 13 (10%) |
| Cardiovascular Symptoms | 11 (8%) |
| NA                | 20 (15%) |
| Presenting laboratory findings | |
| Elevated uric acid | 125 (95%) |
| Elevated creatinine | 112 (85%) |
| Elevated phosphate | 110 (83%) |
| Elevated LDH      | 95 (72%) |
| Elevated potassium | 95 (72%) |
| Low calcium       | 79 (60%) |
| Elevated urea     | 68 (52%) |

Management and Clinical Outcomes

Treatment of TLS was mainly based on hydration (58%; n = 77), allopurinol administration (49%; n = 65), and dialysis (50%; n = 40). However, rasburicase use was reported in 24% of patients (n = 32). The majority (77%, n = 101) of the patients were treated in the ward, while 16% (n = 21) were treated in the ICU. More than half...
(54%, n = 71) of the patients who developed TLS died, and 45% (n = 59) survived (Table 5).

### Table 5: Management and clinical outcomes in reported cases

| Management                  | N (%) |
|-----------------------------|-------|
| IVF                         | 77 (58%) |
| Allopurinol                 | 65 (49%) |
| Dialysis                    | 40 (30%) |
| Diuretics                   | 34 (26%) |
| Rasburicase                 | 32 (24%) |
| Mechanical ventilation      | 10 (8%) |
| Urate oxidase               | 2 (2%) |
| NA                          | 16 (12%) |

| Location         |       |
|------------------|-------|
| Ward             | 101 (77%) |
| ICU              | 21 (16%) |
| ED               | 10 (8%) |

| Outcomes  |       |
|-----------|-------|
| Dead      | 71 (54%) |
| Alive     | 59 (45%) |
| NA        | 2 (2%)  |

IVF: intravenous fluid; NA: not available; ICU: intensive care unit; ED: emergency department

**Discussion**

Our results showed that males aged 58 years are at higher risk for TLS, which is similar to the findings reported by Mirrakhimov et al. [21]. However, we also observed that hepatocellular carcinoma and lung cancer were the most common cancers, in contrast to the findings reported by Mirrakhimov et al. [21]. This is because our review is more up-to-date and the incidence of TLS in solid tumors is increasing due to advancements in novel anti-cancer treatments [22]. Our review demonstrated that metastatic cancer was a major risk factor for TLS, which is similar to the findings reported by Jallad et al. [23] and Vodopivec et al. [24]. Lastly, chemotherapy was the most common anti-cancer treatment attributed to TLS (48%), as reported by Vodopivec et al. (58%) [24].

To the best of our knowledge, this is the first report to address the manifestations of TLS in solid tumors. TLS occurred spontaneously in 24% of the patients and was induced by the treatment in the remaining 76%. Time to TLS development was >5 days following anti-cancer treatment, and 52% of the patients received the full dose of anti-cancer treatment. Additionally, the most commonly reported symptoms were gastrointestinal and genitourinary symptoms in 33% of the patients. The most reported laboratory abnormalities were hyperuricemia (95%), followed by elevated creatinine level (85%), as reported by Vodopivec et al. [24].

In patients with solid tumors who had risk factors for TLS development, large amounts of fluids and allopurinol should be administered before the start of treatment [25]. Once the patient is diagnosed with TLS, treatment should be started using massive amounts of fluids and xanthine oxidase inhibitors such as rasburicase [26]. Our systematic review demonstrated that 58% of patients received intravenous fluids, 49% received allopurinol, and only 24% received rasburicase. These findings illustrate the need for continuous education programs and awareness campaigns to enhance the knowledge of physicians to identify patients at risk and start anti-TLS treatment early and effectively. Moreover, 77% of the patients were treated in the ward, not in the ICU setting. Surprisingly, we found that the mortality rate was 54%, and this is the first report describing the mortality rate associated with TLS in patients with solid tumors. Previous reports evaluating TLS in patients with hematological malignancies described mortality rates ranging from 20% to 50%, with the highest reported rate of 79% in AML patients [27-30].

Our systematic review has several strengths, including the fact that it is the largest and most comprehensive systematic review of case reports describing TLS in patients with solid tumors, manifestations of TLS
following anti-cancer treatment, and the most common symptoms. However, our study also has several limitations: an important caveat for interpreting our study findings is the nature of case reports, since authors report unique cases and the findings may not account for unpublished reports of TLS. One inherent weakness of this study is the limited availability of data in case reports. Another important limitation is that the reporting of the drug dosage, number of doses, and schedule was incomplete in several case reports, and we were unable to determine whether the number of doses influenced the incidence of TLS.

We believe that the management of TLS should focus on risk assessment, prophylaxis, and treatment [31]. Aggressive hydration with oral and intravenous fluids should be initiated before the start of anti-cancer treatment, and oral hydration and adequate urine output should be maintained for several days after the completion of the treatment [32]. Urate-lowering agents, such as allopurinol or rasburicase, are recommended for prophylaxis and management of TLS [26]. Febuxostat is also a urate-lowering agent that can provide better control of hyperuricemia in TLS with a good safety profile if allopurinol is contraindicated or not available.

The findings show that TLS is a lethal condition, and early identification with prompt initiation of preventative measures is essential to save patient lives. Although the data indicated modest prognostic benefits, early initiation of anti-TLS measures will improve oncological outcomes. Care of patients with TLS requires an interdisciplinary approach including nephrologists, intensivists, oncologists, and internists in closed observation units, such as intermediate care or ICUs [33,34].

Conclusions
In this systematic review, we found that older men had a higher tendency to develop TLS. Hepatocellular carcinoma was the most common type of cancer leading to TLS development, followed by lung cancer and melanoma. Metastatic cancer was a contributing risk factor for TLS development. Chemotherapy was the most common class of anti-cancer treatment that induced TLS. Manifestations of TLS developed within ≥3 days following anti-cancer treatment, and half of the patients received the full dose of anti-cancer treatment. Gastrointestinal and genitourinary symptoms were the most commonly reported, and almost all patients showed high uric acid and elevated creatinine levels.

Appendices
Appendix 1

| Pubmed: | Keywords |
|---------|----------|
| #       |          |
| 1       | "tumor lysis syndrome" |
| 2       | "spontaneous tumor lysis syndrome" |
| 3       | "Acute tumor lysis syndrome" |
| 4       | "tumour lysis syndrome" |
| 5       | OR/1-4 |
| 6       | ("Solid tumor" OR "Solid cancer" OR "solid carcinoma" OR "solid neoplasm") |
| 7       | ("breast cancer" OR "breast carcinoma") |
| 8       | ("lung cancer" OR "lung carcinoma") |
| 9       | ("liver cancer" OR "hepatic carcinoma") |
| 10      | ("ovarian cancer" OR "ovarian carcinoma" OR "ovarian tumor") |
|         | ("colon cancer" OR "colon carcinoma" OR "colon tumor") |
| 11      | ("gastric cancer" OR "gastric tumor") |
| 12      | ("Brain cancer" OR "brain tumor") |
| 13      | ("prostate cancer" OR "prostate tumor")/"skin tumor" |
| 14      | "skin tumor" |
| 15      | sarcoma |
| 16      | ("bone cancer" OR "bone carcinoma") |
| 17      | ("pancreatic cancer" OR "pancreatic carcinoma" OR "pancreatic tumor") |
| 18      | "cervical cancer" |
20  "cervix carcinoma"
21  ("endometrial cancer" OR "endometrial tumor" OR "endometrial adenocarcinoma")
22  ("esophageal cancer" OR "esophageal tumor")
23  ("hepatocellular cancer" OR "hepatocellular carcinoma") ("small cell cancer" OR "small cell carcinoma" OR "small cell tumor")
24  ("small cell cancer" OR "small cell carcinoma" OR "small cell tumor")
25  ("germ cell cancer" OR "germ cell tumor")
26  osteosarcoma
27  neuroblastoma
28  medulloblastoma
29  ("renal cancer" OR "renal carcinoma" OR "renal cell cancer" OR "renal cell carcinoma" OR "renal cell tumor")
30  mesothelioma
31  glioblastoma
32  melanoma
33  OR/6-32
34  5 AND 33
35  English
36  Human
37  Adult(+19)
38  OR 35-37
39  34 And 38

Ovid:
#             Keywords
1             All of resources were selected except books
2             "tumor lysis syndrome"
3             "spontaneous tumor lysis syndrome"
4             "Acute tumor lysis syndrome"
5             "tumour lysis syndrome"
6             OR/2-5
7             ("Solid tumor" OR "Solid cancer" OR "solid carcinoma" OR "solid neoplasm")
8             ("breast cancer" OR "breast carcinoma")
9             ("lung cancer" OR "lung carcinoma")
10            ("liver cancer" OR "hepatic carcinoma")
11            ("ovarian cancer" OR "ovarian carcinoma" OR "ovarian tumor")
12            ("colon cancer" OR "colon carcinoma" OR "colon tumor")
13            ("gastric cancer" OR "gastric tumor")
14            ("Brain cancer" OR "brain tumor")
15            ("prostate cancer" OR "prostate tumor")
16            "skin tumor"
17            sarcoma
18            ("bone cancer" OR "bone carcinoma")
19            ("pancreatic cancer" OR "pancreatic carcinoma" OR "pancreatic tumor")
| 20 | “cervical cancer” |
| 21 | “cervix carcinoma” |
| 22 | (“endometrial cancer” OR “endometrial tumor” OR “endometrial adenocarcinoma”) |
| 23 | (“esophageal cancer” OR “esophageal tumor”) |
| 24 | (“hepatocellular cancer” OR “hepatocellular carcinoma”) |
| 25 | (“small cell cancer” OR “small cell carcinoma” OR “small cell tumor”) |
| 26 | (“germ cell cancer” OR “germ cell tumor”) |
| 27 | Osteosarcoma |
| 28 | neuroblastoma |
| 29 | medulloblastoma |
| 30 | (“renal cancer” OR “renal carcinoma” OR “renal cell cancer” OR “renal cell carcinoma” OR “renal cell tumor”) |
| 31 | mesothelioma |
| 32 | glioblastoma |
| 33 | Melanoma |
| 34 | OR/7-33 |
| 35 | 6 AND 34 |
| 36 | D duplicates from ovid |
| 37 | English |
| 38 | Human |
| 39 | Adult(+19) |
| 40 | OR 36-39 |
| 41 | 35 And 40 |

Cochrane library:
| 1 | “tumor lysis syndrome” |
| 2 | “spontaneous tumor lysis syndrome” |
| 3 | “Acute tumor lysis syndrome” |
| 4 | “tumour lysis syndrome” |
| 5 | OR/1-4 |
| 6 | (“Solid tumor” OR “Solid cancer” OR “solid carcinoma” OR “solid neoplasm”) |
| 7 | (“breast cancer” OR “breast carcinoma”) |
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| 9 | (“liver cancer” OR “hepatic carcinoma”) |
| 10 | (“ovarian cancer” OR “ovarian carcinoma” OR “ovarian tumor”) |
| 11 | (“colon cancer” OR “colon carcinoma” OR “colon tumor”) |
| 12 | (“gastric cancer” OR “gastric tumor”) |
| 13 | (“Brain cancer” OR “brain tumor”) |
| 14 | (“prostate cancer” OR “prostate tumor”) |
| 15 | “skin tumor” |
| 16 | sarcoma |
| 17 | (“bone cancer” OR “bone carcinoma”) |
| 18 | (“pancreatic cancer” OR “pancreatic carcinoma” OR “pancreatic tumor”) |
| 19 | “cervical cancer” |
20 "cervix carcinoma"
21 ("endometrial cancer" OR "endometrial tumor" OR "endometrial adenocarcinoma")
22 ("esophageal cancer" OR "esophageal tumor")
23 ("hepatocellular cancer" OR "hepatocellular carcinoma")
24 ("small cell cancer" OR "small cell carcinoma" OR "small cell tumor")
25 ("germ cell cancer" OR "germ cell tumor")
26 osteosarcoma
27 neuroblastoma
28 medulloblastoma
29 ("renal cancer" OR "renal carcinoma" OR "renal cell cancer" OR "renal cell carcinoma" OR "renal cell tumor")
30 mesothelioma
31 glioblastoma
32 Melanoma
33 OR/ 6-32
34 5 AND 33

**TABLE 6: Search methodology**

| Author          | Year   | Title         | Demographics (age, sex) | Current health status | Medical history | Physical exam | Patient disposition | Drug identification | Dosage | Drug reaction interface | Concomitant therapy | Adverse events | Discuss |
|-----------------|--------|---------------|-------------------------|-----------------------|-----------------|---------------|--------------------|--------------------|--------|------------------------|--------------------|---------------|---------|
| Katiman         | 2012   |               | Yes                     | Yes                   | Yes             | Yes           | Yes                 | Yes                 | Yes    | No                     | Yes                | Yes           |         |
| Kekre           | 2012   |               | Yes                     | Yes                   | Yes             | Yes           | Yes                 | No                  | No     | No                     | No                 | Yes           |         |
| Mouallem        | 2013   |               | Yes                     | Yes                   | Yes             | Yes           | Yes                 | Yes                 | No      | Yes                    | Yes                | Yes           |         |
| Durham          | 2017   |               | Yes                     | Yes                   | Yes             | Yes           | Yes                 | No                  | Yes    | No                     | No                 | No            |         |
| D’Alessandro     | 2010   |               | Yes                     | Yes                   | Yes             | Yes           | Yes                 | No                  | No     | No                     | No                 | Yes           |         |
| Drakos          | 1994   |               | Yes                     | Yes                   | Yes             | Yes           | Yes                 | Yes                 | Yes    | No                     | Yes                | Yes           |         |
| Tomlinson       | 1984   |               | Yes                     | Yes                   | Yes             | Yes           | Yes                 | Yes                 | Yes    | Yes                    | Yes                | Yes           |         |
| Marinella       | 1999   |               | Yes                     | Yes                   | Yes             | Yes           | Yes                 | Yes                 | Yes    | Yes                    | Yes                | Yes           |         |
| Castro          | 1999   |               | Yes                     | Yes                   | Yes             | Yes           | Yes                 | Yes                 | Yes    | Yes                    | Yes                | Yes           |         |
| Han             | 2008   |               | Yes                     | Yes                   | Yes             | Yes           | Yes                 | Yes                 | Yes    | No                     | Yes                | Yes           |         |
| Lehner          | 2005   |               | Yes                     | Yes                   | Yes             | Yes           | Yes                 | Yes                 | Yes    | Yes                    | Yes                | Yes           |         |
| Sklarin         | 1995   |               | Yes                     | Yes                   | Yes             | Yes           | Yes                 | Yes                 | Yes    | No                     | No                 | Yes           |         |
| Borne           | 2009   |               | Yes                     | Yes                   | No              | Yes           | Yes                 | Yes                 | Yes    | Partial                | Yes                | Yes           |         |
| Author          | Year | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | Yes   |
|-----------------|------|-------|-------|-------|-------|-------|-------|-------|-------|------|-------|-------|
| Hsieh 2009      |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | Yes   |
| Kim 2017        |      | Yes   | Yes   | Yes   | Yes   | Partial | Yes   | No   | No   | No   | No   | Yes   |
| van Kalleveen   | 2018 | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | Yes   |
| Vaidya 2015     |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | Yes   |
| Baeksgaard 2003 |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | Yes   |
| Farooqi 2015    |      | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | No   | No   | No   | Yes   |
| Gbaguidi 2016   |      | Yes   | Yes   | Yes   | Yes   | Partial | Yes   | No   | NO   | NO   | NO   | NO   | Yes   |
| Bilgrami 1993   |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | Yes   |
| Camarata 2013   |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | Yes   |
| Geum 2008       |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | Yes   |
| Blanke 2000     |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | Yes   |
| Wang 2010       |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | No   | Yes   | Yes   |
| Bhardwaj 2018   |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | Yes   |
| Ajzensztejn 2006|      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | Yes   |
| Chan 2005       |      | Yes   | Yes   | Yes   | No   | Yes   | Yes   | Yes   | No   | Yes   | No   | Yes   |
| Baudon 2016     |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Partial | Yes   | No   | Yes   |
| Berwal 2002     |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Partial | Yes   | No   | Yes   |
| Godoy 2010      |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | No   | Yes   |
| Gongona 2019    |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Partial | Yes   | No   | Yes   |
| Gold 1993       |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | No   | Yes   | No   | Yes   |
| Yoshimura 2008  |      | Yes   | Yes   | No   | Yes   | Yes   | Yes   | No   | No   | No   | No   | yes   |
| Boikos 2013     |      | Yes   | Yes   | Yes   | No   | Yes   | Yes   | Yes   | Partial | Yes   | No   | Yes   |
| Dar 2014        |      | Yes   | Yes   | Yes   | No   | Yes   | Yes   | Yes   | Partial | Yes   | No   | Yes   |
| Woo 2001        |      | Yes   | Yes   | Yes   | Yes   | Yes   | No   | No   | No   | No   | No   | No   |
| Vogelzang 1983  |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Partial | Yes   | No   | Yes   |
| Yahata 2008     |      | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   | Yes   |
| Chao 2012       |      | Yes   | Yes   | Yes   | Yes   | No   | No   | No   | Yes   | No   | Yes   | Yes   |
| Author | Yes | Yes | Yes | Yes | No | Yes | No | Yes | Yes | Yes | No | Yes | Yes |
|--------|-----|-----|-----|-----|----|-----|----|-----|-----|-----|----|-----|-----|
| Baumann 1983 [58] | Yes | Yes | Yes | Yes | No | Yes | No | Yes | Yes | Yes | No | Yes | Yes |
| Abbass 2011 [59] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | No |
| Vishwanathan 2019 [60] | No | Yes | Yes | Yes | Yes | Yes | No | No | No | No | Yes | Yes |
| Stoves 2001 [61] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | No |
| Tsai 2012 [62] | Yes | Yes | Yes | Yes | Yes | Yes | No | No | Yes | No | Yes | Yes |
| Hirai 2011 [63] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Partial | Yes | No | Yes | Yes |
| Henrich 2008 [64] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Hussein 1990 [65] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Burney 1998 [66] | Yes | Yes | Yes | Yes | Yes | Yes | Partial | Partial | No | Yes | Yes |
| Chian 2015 [67] | Yes | Yes | Partial | Yes | No | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Agarwala 2017 [68] | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | Yes | Yes |
| Catania 2017 [69] | Yes | Yes | Yes | Yes | No | No | No | No | No | No | Yes | Yes |
| Ignaszewski 2017 [70] | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | Yes | Yes |
| Jallad 2011 [71] | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | Yes | Yes |
| Stuart 2017 [72] | Yes | Yes | partial | Yes | Yes | Yes | Yes | Yes | No | Yes | No | Yes | Yes |
| Jiang 2016 [73] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes |
| Kallab 2001 [74] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes |
| Kaplan 2012 [75] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes |
| Sewani 2002 [76] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes |
| Sakamoto 2007 [77] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes |
| Taira 2015 [78] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | No | Yes | Yes |
| Sorscher 2004 [79] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes |
| Shibata 2008 [80] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes |
| Ragnault 2016 [81] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes |
| Wright 2005 [82] | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | Yes | partial |
| Weil 2018 [83] | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | Yes | Yes |
| Mazzoni 2016 [84] | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | No | Yes | Yes | Yes |

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| Study                      | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
|---------------------------|-----|-----|-----|-----|-----|-----|-----|-----|----|-----|-----|
| Krishnan 2008             | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Lee 2006                  | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | No | Yes |
| Salem 2015                | Yes | Yes | Yes | Yes | Yes | No | No | No | No | Yes | Yes |
| Zigrossi 2001             | No  | Yes | No  | No  | Yes | Yes | No | No | No | Yes | No  |
| Kalenderian 1997          | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Habib 2002                | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Stark 1987                | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Meeks 2016                | Yes | Yes | Yes | No  | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Busam 2004                | Yes | Yes | Yes | No  | Yes | Partial | Yes | Yes | No | No | Yes |
| Mehrzad 2014              | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | Yes |
| Michels 2010              | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Nakamura 2009             | Yes | Yes | Yes | No  | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Gouveia 2018              | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Partial | No | No | Yes |
| Huang 2009                | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Lin 2007                  | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | Yes |
| Nicholas 2007             | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | Yes |
| Norberg 2014              | Yes | Yes | Yes | No  | Yes | No  | No  | No  | No  | Yes | Yes |
| Oztop 2004                | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Pabon 2018                | Yes | Yes | Partial | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Pindak 2019               | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Rostom 2000               | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Romo 2019                 | Yes | Yes | Yes | No  | Yes | Yes | Yes | Yes | No | No | No  |
| Okay 2019                 | Yes | Yes | Yes | No  | Yes | Yes | Yes | Yes | No | partial | No | No | No |
| Dhakal 2018               | Yes | Yes | Yes | Yes | Yes | No | No | No | No | Yes | Yes |
| Shizawa 2010              | Yes | Yes | Yes | No  | Yes | No  | Yes | No  | Partial | Yes | No | No |
| Dirix 1991                | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |
| Shamseddine. 1993         | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Partial |
| Reference          | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | Yes | Yes |
|--------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|----|----|----|-----|-----|
| Song, 2011         |     |     |     |     |     |     |     |     |     | Yes| Yes| Yes| Yes| Yes | Yes |
| Takeuchi, 2016     | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | No | Yes | Yes |
| Kim, 2014          | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Partial | Yes | No | Yes | Yes | Yes |
| Chow, 2015         | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | No | Yes | Yes | Yes | Yes |
| Cech, 1986         | No  | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes |
| Feld, 2000         | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | No | Yes | Yes | Yes | Yes |
| Boisseau, 1996     | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | No | Yes | No |
| Alaigh, 2017       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes |
| Pinder, 2007       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes |
| Kurt, 2005         | Yes | Yes | Yes | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Kawai, 2006        | Yes | Yes | Yes | No | Yes | Yes | Yes | No | Yes | No | Yes | Yes | Yes | Yes | Yes |
| Vaisban, 2003      | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | No | Yes | Yes | Yes |
| Okamoto, 2015      | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | No | Yes | Yes | Yes | Yes |
| Boyd, 2017         | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | No | Yes | Yes | Yes | Yes |
| Vodopivec, 2012   | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | No | Yes | Yes | Yes | Yes | Yes |
| Tseng, 2016        | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes |
| Berringer, 2017    | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | No | Yes | Yes | Yes | Yes |
| Sommerhalder, 2017 | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | No | Yes | Yes | Yes | Yes |
| Shenoy, 2009       | Yes | Yes | Yes | Yes | Yes | Yes | No | No | No | No | No | Yes | Yes | Yes | Yes |
| Lee, 2013          | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes |
| Tamvetyanon, 2004  | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes |
| Ustundag, 1997     | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Partial | Yes | No | Yes | Yes | Yes | Yes |
| Abbouda, 2009      | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes |
| Barton, 1989       | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes |
| Mott, 2005         | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Partial | Yes | No | Yes | Yes | Yes | Yes |
| Qian, 2009         | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes |
### TABLE 7: Quality assessment of included studies

| Case (Author, year, reference no.) | Age (years) | Gender (M/F) | Primary cancer | Anti-cancer treatment: Full dose or reduced (class and name) | Number of doses: days preceding presentation | Any comorbidities | Presenting symptoms | Risk factors |
|-----------------------------------|-------------|--------------|----------------|-------------------------------------------------------------|-----------------------------------------------|-------------------|---------------------|-------------|
| Katiman, 2012 [2]                | 55          | M            | HCC            | chemotherapy: TACE (doxorubicin)                            | 1 cycle: 1 dose: 1 day after initiation         | HTN, hepatitis B| right hypochondrial pain, nausea, haematuria. | bulky tumor   |
| Kekre, 2012 [3]                  | 76          | M            | HCC            | spontaneous                                                | none                                          | hemochromatosis, arthritis, DM, CKD, HTN, dyslipidemia, erectile dysfunction. | nausea, vomiting, diarrrhea, epigastric pain, and decreased appetite. | bulky tumor, pre-existing renal compromise. |
| Mouallem, 2013 (Case 1) [4]      | 68          | M            | melanoma       | chemotherapy: dacarbazine                                   | 3 courses: 3 days after the last course         | N/A               | nausea, vomiting, weakness, confusion and oliguria | bulky and metastatic tumor |
| Mouallem, 2013 (Case 2) [4]      | 69          | M            | melanoma       | spontaneous                                                | N/A                                           | N/A               | rectal bleeding                             | bulky and metastatic tumor |
| Durham, 2018 [5]                 | 59          | M            | melanoma       | spontaneous                                                | N/A                                           | N/A               | abdominal pain, nausea                      | metastatic tumor |
| D’Alessandro, 2010 [6]           | 22          | M            | germ cell tumor| spontaneous                                                | N/A                                           | DM                | abdominal fullness, epigastric pain, weight loss and lethargic | metastatic tumor |
| Drakos, 1994 [7]                 | 32          | F            | breast carcinoma| Chemotherapy: mitoxantrone 14 mg/m2: 22 mg, full dose      | 1 cycle: 2 doses: 4 days after initiation.      | N/A               | nausea, vomiting, abdominal pain, confusion | rapidly growing tumors with spreading to other organ, and pretreatment high LDH |
| Tomlinson, 1984 [8]              | 34          | F            | medulloblastoma| Radiotherapy: cobalt-60 100 radiation per day, full dose    | fourth day after total of 300 radiation         | N/A               | oliguria                                    | metastatic cancer, pretreatment high LDH |
| Marinella, 1999 [9]              | 52          | M            | SCLC           | Chemotherapy: etoposide (100 mg/m2) and cisplatin 30 mg/m2, full dose | 1 cycle: 1 days after initiation              | DM and HTN        | lethargic, hematochezia                      | metastatic tumor |
| Castro, 1999 [10]                | 61          | M            | melanoma       | Biochemotherapy: interleukin-2 MIU/M2/day IV, interferon-α 5MIU/M2/day SQ, dacarbazine 800mg/m2/day, | 1 cycle: 4 days after initiation              | N/A               | oliguria                                    | metastatic and bulky tumor |
| Study            | Age | Sex  | Tumor Location    | Treatment Description                                      | Toxicity                      | Toxicity Description                                      |
|------------------|-----|------|-------------------|------------------------------------------------------------|-------------------------------|-----------------------------------------------------------|
| Han, 2008 [11]  | 38  | M    | gastric cancer    | vinblastine 1.6mg/m2/day IV, cisplatin 20mg/m2/day IV, full dose | N/A                           | bulky and metastatic tumor                                |
|                  |     |      |                   |                                                             |                               | pretreatment high LDH and the tumor is highly sensitive to chemotherapy |
| Lehnar, 2005 [12]| 64  | M    | HCC               | radiofrequency ablation 2 portions of ablation: 2 days after initiation | N/A                           | hypoxia dyspnea, oliguria, arrhythmia                      |
|                  |     |      |                   |                                                             |                               | bulky                                                     |
| Sikarin. 1995 [13]| 62  | F    | breast cancer     | spontaneus                                                  | N/A                           | dyspnea                                                   |
|                  |     |      |                   |                                                             |                               | metastatic cancer, high baseline LDH                      |
| Borne, 2009 [14] | 42  | M    | melanoma          | corticosteroid high dose 48 hours after initiation          | N/A                           | N/A                                                       |
|                  |     |      |                   |                                                             |                               | metastatic cancer, bulky tumor                            |
| Hsieh (case 1), 2009 [15] | 76  | F    | HCC               | chemotherapy: TACE with 20 mg adriamycin, full dose 1 cycle: 1 dose: 3 days after initiation | N/A                           | acute renal insufficiency                                 |
|                  |     |      |                   |                                                             |                               | N/A                                                       |
| Hsieh (case 2), 2009 [15] | 56  | M    | HCC               | chemotherapy: TACE with 10 mg of lipiodol + 20 mg adriamycin, full dose 1 cycle: 1 dose: same night of TACE initiation. | hepatitis B                  | oliguria                                                  |
|                  |     |      |                   |                                                             |                               | N/A                                                       |
| Kim, 2017 [17]  | 35  | F    | cervical cancer   | spontaneus                                                  | N/A                           | general weakness                                          |
| van Kalleveen, 2018 [18] | 58  | M    | RCC               | targeted therapy: pazopanib 800mgm, full dose 1 cycle: 6 days after administration | N/A                           | nausea, vomiting and diarrhea                            |
|                  |     |      |                   |                                                             |                               | metastatic cancer                                         |
| Vaidya, 2015 [35]| 52  | F    | breast cancer     | chemotherapy: paclitaxel 80mg/m2, full dose 1 cycle: 1 dose: 1 week after administration | N/A                           | confusion and sluggishness                                 |
|                  |     |      |                   |                                                             |                               | metastatic cancer                                         |
| Baeksgaard, 2003 [25] | 23  | M    | medulloblastoma   | chemotherapy (cisplatin 20mg/m2, etoposide 50mg/m2) for five days every 3 weeks full dose 1 cycle 2 dose 2 days after initiation | N/A                           | fatigue, difficulty in breathing, and low urine output    |
|                  |     |      |                   |                                                             |                               | pretreatment high LDH, and metastatic cancer              |
| Farooqi 2015 [36] | 52  | M    | colorectal cancer (cecum) | targeted therapy (regorafenib) 1 week after initiation | HTN, asthma, and recent stroke | nausea, and vomiting                                      |
|                  |     |      |                   |                                                             |                               | metastatic tumor                                          |
| Gibaguidi, 2016 [37] | 88  | F    | RCC               | spontaneus                                                  | N/A                           | HTN, heart failure, and CKD                               |
|                  |     |      |                   |                                                             |                               | vomiting                                                  |
|                  |     |      |                   |                                                             |                               | bulky and metastatic tumor, acute medical condition (infection). |
| Bilgrami , 1993 [38] | 47  | F    | Advanced ovarian cancer | combination chemotherapy: carboplatin 400mg/m2 and cyclophosphamide 1 cycle: 1 dose: 4 days after initiation | N/A                           | bulky and rapidly growing tumors                           |
| Study, Year | Age | Gender | Diagnosis | Treatment Details | Followup | Side Effects | Metastatic/Tumor Status |
|------------|-----|--------|-----------|-------------------|----------|-------------|------------------------|
| Camarata, 2013 [39] | 63 F | | serous ovarian cancer | 500mg/m², full dose | combination chemotherapy: carboplatin and paclitaxel 75mg/m², full dose | 1 cycle: 1 dose: 2 days after initiation | high output heart failure | bulky and metastatic tumor |
| Geun, 2008 [40] | 52 M | | NSCLC | palliative radiotherapy: total dosage of 30 Gy divided by 10 fractions, full dose | second fractions (total of 60Gy) | | | |
| Blanke, 2000 [41] | 52 M | | Choriocarcinoma | Chemotherapy: etoposide 100mg/m² and cisplatin 20mg/m², full dose | | 1 cycle: 2 days after initiation | HTN, osteoarthritis, hypercholesterolemia, oliguria | metastatic cancer, pretreatment high LDH |
| Wang, 2010 [42] | 54 F | | HCC | chemotherapy: TACE with doxorubicin 60 mg and lipiodol 20ml, full dose | | 1 cycle: 1 dose: 5 days after initiation. | | decreased urine output |
| Bhardwai, 2018 [43] | 67 M | | prostatic cancer | Chemotherapy: docetaxel 75 mg/m², full dose | | 1 cycle: 1 dose: 3 days after initiation | | |
| Ajzensztejn, 2006 [44] | 65 M | | NSCLC | Chemotherapy: docetaxel 75 mg/m², full dose | | 1 cycle: 1 dose: 3 days after initiation | COPD | metastatic cancer, and large tumor burden |
| Chan, 2005 [45] | 62 F | | ovarian cancer | Chemotherapy: topotecan | | 2 cycle 2 weeks after initiation | | |
| Baudon, 2016 [46] | 58 F | | breast cancer | target therapy: trastuzumab, pertuzumab | | 1 cycle: 2 days after her first course | TB | hypovolemic shock |
| Beriwal, 2002 [47] | 68 M | | SCLC | chemotherapy: topotecan | | 1 cycle: 1 dose: 1 day after initiation | | low urinary output 200ml |
| Godoy, 2010 [48] | 60 F | | endometriat cancer | chemotherapy: carboplatin, paclitaxel | | 1 cycle: 4 days after initiation | | shortness of breath, weakness, and fatigue |
| Gongora, 2019 [49] | 46 M | | prostatic cancer | chemotherapy: carboplatin, etoposide | | 5 days after initiation | | |
| Gold 1993 [50] | 66 M | | gastric leiomyosarcoma | chemotherapy: cyclophosphamide 2 g/m²; immunotherapy: autolymphocyte therapy, full dose | | 1 cycle: 1 dose: 16 hours after initiation of the adaptive chemoimmunotherapy | HTN | nausea, fever, and abdominal pain |
| Yoshimura, 2019 | 59 M | | gastric cancer | Chemotherapy: irinotecan and 5-fluorouracil | | After second cycle of | N/A | mild edema of the |
| Year  | Age | Gender | Site            | Treatment                                                                 | Duration                                                                 | Side Effects                                                                 | Diagnosis               |
|-------|-----|--------|-----------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------|-------------------------|
| 2008  | 70  | F      | SCLC            | chemotherapy: cisplatin, etoposide                                        | 1 cycle: 8 days after initiation                                          | N/A                                                                       | legs                    |
| Boikos, 2013 | 65  | M      | melanoma        | palliative radiotherapy                                                    | 5 radiation sessions 7 days after the last session                        | N/A                                                                       | general illness, renal insufficiency metastatic cancer                   |
| Dar, 2014 | 36  | M      | gastric cancer  | spontaneous                                                               |                                                                           | N/A                                                                       | abdominal fullness and pain metastatic cancer                         |
| Woo, 2001 | 57  | F      | SCLC            | chemotherapy: docorubicin50% dose reduction, cisplatin, etoposide, and vincristine sulfate | 1 cycle: 1 dose: 36 hours after initiation                                | N/A                                                                       | respiratory distress metastatic cancer                                |
| Vogelzang, 1983 | 53  | M      | ovarian cancer  | paclitaxel 100mg, full dose                                               | 5 days after administration                                               | N/A                                                                       | oliguria N/A             |
| Yahata, 2006 | 51  | M      | HCC             | chemotherapy: TACE; type of drugs use not mentioned                       |                                                                           | N/A                                                                       | abdominal pain, oliguria, and fever N/A                                |
| Chao, 2012 | 78  | M      | SCLC            | chemotherapy: doxorubicin 30mg, cyclophosphamide 900mg, vincristine 2.0mg, full dose | 7 days after initiation                                                   | N/A                                                                       | oliguria metastatic cancer                                             |
| Baumann, 1983 | 53  | M      | melanoma        | sorafenib 800 mg/day, full dose                                           | 7 days after initiation                                                   | hepatitis B                                                              | somnolent, and pretreatment high LDH                                    |
| Abbass, 2011 | 43  | M      | HCC             | chemotherapy and immunotherapy: cisplatin 30mg/m2 and dacarbazine 250mg/m2 on days 1-3 and interferon alpha 10MU/m2 on days 1-5 of treatment, full dose | 1 cycle: 2 days after initiation                                          | N/A                                                                       | oliguria ascites metastatic cancer                                     |
| Vishwanathan, 2019 | 51  | M      | uterine cancer  | spontaneous                                                               |                                                                           | N/A                                                                       | fatigue, weakness, abdominal girth and pain, vaginal spotting, and hematuria N/A |
| Stoves, 2001 | 36  | F      | HCC             | chemotherapy and TACE; name of drugs and doses not mentioned             |                                                                           | N/A                                                                       | large tumor burden                                                    |
| Tsai, 2012 | 62  | M      | melanoma        | chemotherapy: PVE and TACE; name of drugs and doses not mentioned        | 1 cycle: 2 days after initiation                                          | hepatitis B                                                              | large, bulky and metastatic cancer pretreatment high LDH               |
| Hiraiuzumi, 2011 | 62  | M      | uterine leiomyosarcoma | chemotherapy: vincristine, actinomycin-D, and cyclophosphamide           | 2 cycle: 7 days after the second cycle of chemotherapy                   | N/A                                                                       | confused and decreased urine output large, bulky and metastatic cancer |
| Hentrich, 2008 | 36  | F      | colon cancer    | chemotherapy and target therapy: bevacizumab 5 mg/kg IV, irinotecan 50   | 1 cycle: 2 days after                                                    | N/A                                                                       | metastatic cancer                                                   |
| Reference       | Age | Gender | Diagnosis | Chemotherapy Details                                                                 | Course Details | Side Effects                                                                 |
|-----------------|-----|--------|-----------|--------------------------------------------------------------------------------------|----------------|-------------------------------------------------------------------------------|
| Hussein, 1990   | 57  | M      | SCLC      | Chemotherapy: cyclophosphamide 750 mg/m², doxorubicin 45 mg/m², and vincristine 2 mg (all intravenously), full dose | 1 cycle: 4 days after chemotherapy started | N/A               |
| Burney, 1998 (case 1) | 44  | M      | HCC       | Chemotherapy: TACE (cisplatin 60 mg/m²), full dose | 1 cycle: 1 dose 8 hours after infusion | oliguria N/A         |
| Burney, 1998 (case 2) | 46  | M      | HCC       | Chemotherapy: TACE, drugs not mentioned | N/A | N/A                                                                         |
| Cihan, 2015     | 61  | M      | unknown primary tumor | Chemotherapy: cetuximab 400mg/m², irinotecan 125mg/m², full dose | 1 cycle: 1 dose 16 hours after infusion | N/A               |
| Agarwala, 2017  | 26  | F      | HCC       | spontaneous | N/A | hepatitis B                   |
| Catania, 2017   | 65  | F      | ESOS      | spontaneous | N/A | abdominal pain |
| Ignaszewski, 2017 | 69 | M | prostate adenocarcinoma | spontaneous | N/A | HTN, hyperlipidemia |
| Jallad, 2011 | 75 | F | SCLC | spontaneous | TLS appeared 3 days following radiotherapy | N/A               |
| Stuart, 2017    | Mid | M      | BAC       | palliative radiotherapy | N/A | seizure and global weakness |
| Jiang, 2016     | 52  | M      | HCC       | Chemotherapy: TACE (iodised oil 20 ml with 5-fluorouracil 500 ml, epirubicin 30 mg) | 1 cycle: 1 dose: 1 day after TACE | liver cirrhosis and chronic hepatitis B virus |
| Kallab, 2001    | 61  | M      | SCLC      | Chemotherapy: cisplatin 80 mg/m² on day 1 and etoposide 120 mg/m² on day 1-3, full dose | 1 cycle: 1 dose of cisplatin and 3 doses of etoposide 4 days after initiation of chemotherapy | N/A               |
| Kaplan, 2012    | 60  | M      | prostate cancer | Palliative radiotherapy: total of 30 Gy radiotherapy in 10 fractions, full dose | Day 3 of radiotherapy | oliguria and dyspnea |

**Chemotherapy: 1 cycle: 1 dose:**

** Pretreatment high LDH: metastatic cancer, pretreatment high LDH

** Pretreatment high LDH: metastatic cancer, metastatic cancer, metastatic cancer, metastatic cancer, high tumor burden and metastatic cancer.
| Name            | Year | Gender | Diagnosis          | Treatment Description                                                                 | Duration | Side Effects                                      | Cancer Type |
|-----------------|------|--------|--------------------|---------------------------------------------------------------------------------------|----------|--------------------------------------------------|-------------|
| Sewani, 2002    |      | M      | mixed SCLC and NSCLC | carboplatin 830 mg, paclitaxel 440 mg, full dose                                       | 1 day    | Abdominal pain and fever                          | metastatic  |
| Sakamoto, 2007  |      | M      | HCC                | chemotherapy: TOCE (15 mL of iodized oil, 50 mg of epirubicin hydrochloride, and embolization with two sheets of gelatin sponge) | 2 cycles | hepatitis B, fever, decrease urine output, severe diarrhea, anuria cough, hemoptysis, and dyspnea, bulky tumor with high LDH level before TOCE |           |
| Taira, 2015     | 69   | F      | breast cancer      | targeted therapy: trastuzumab                                                         | 1 cycle  | cardiac arrhythmia                               | -metastatic |
| Sorscher, 2004  | 80   | M      | Prostate cancer    | chemotherapy: docetaxel at 35 mg/m2, full dose                                         | 1 cycle  | N/A                                              | -Metastatic |
| Shiba, 2008     | 77   | M      | HCC                | chemotherapy: TACE (hydrochloric acid epirubicin 70 mg, 20 mL of iodized oil esters, and 160 mg of porous gelatine grains, full dose) | 1 cycle  | fatigue, fever and oliguria                       | large tumor burden |
| Regnault, 2016  | 73   | M      | nodular melanoma   | Immunotherapy: Ipilimumab                                                             | 1 cycle  | cardiac arrhythmia                               | Metastatic   |
| Wright, 2005    | 60   | M      | prostate cancer    | chemotherapy: paclitaxel 100 mg/m2, full dose                                          | 1 cycle  | anuria                                           | metastatic  |
| Weil, 2018      | 64   | F      | small cell carcinoma of the cervix | spontaneous                                                                           | N/A      | DM, HTN, dyslipidemia, weakness, fatigue and abdominal pain, high pretreatment LDH and metastatic cancer |
| Mazzoni, 2016   | 62   | M      | prostate cancer    | palliative radiotherapy: external beam radiation therapy, TURP, and hormonal therapy (bicatalumide) | N/A      | fatigue, weakness, confusion and anuric           | metastatic  |
| Krishnan, 2008  | 64   | M      | colon cancer       | targeted therapy: cetuximab 400mg/m2, full dose                                       | 1 cycle  | N/A                                              | metastatic  |
| Lee, 2006       | 62   | M      | HCC                | immuno-target therapy: thalidomide 300mg per day, full dose                            | 1 cycle  | SOB                                              | N/A         |
| Saleh, 2015     | 56   | F      | pancreatic cancer  | spontaneous                                                                           | N/A      | generalised weakness                             | metastatic  |
| Zigrossi, 2001  |      | F      | breast cancer      | hormonal therapy: letrozole                                                           | N/A      | shock, bilateral pleural effusion, cardiac tamponade, and oliguria | N/A         |
| Kalemkerian,     |      |        |                    | Chemotherapy: cisplatin 80 mg/m2 on day 1 and                                         | 1 cycle  | lethargic and                                    | metastatic tumor and |
| Year       | Age | Gender | Diagnosis            | Treatment                                                                 | Symptoms                                    | Details                                                                 |
|------------|-----|--------|----------------------|---------------------------------------------------------------------------|---------------------------------------------|-------------------------------------------------------------------------|
| Kalemkerian, 1997 [88] | 74  | F      | SCLC                 | chemotherapy: cisplatin 80 mg/m2 on day 1 and etoposide 100 mg/m2 on days 1 to 3, full dose | lethargic and oliguric                       | metastatic tumor and pretreatment high LDH                               |
| Stark, 1987 [90] | 53  | F      | breast adenocarcinoma | Chemotherapy: fluorouracil 400 mg/m2, doxorubicin 40 mg/m2, cyclophosphamide 400 mg/m2, full dose | N/A                                         | metastatic cancer, rapidly growing tumors, pretreatment high LDH, and high tumor burden |
| Meeks, 2016 [91] | 46  | M      | unknown primary cancer | Steroid: dexamethasone 4 mg per 6 hours, full dose | 2 days after initiation | anemia, lower back pain                                                  | metastatic cancer and bulky tumor                                       |
| Stark, 1987 [90] | 53  | F      | breast adenocarcinoma | Chemotherapy: fluorouracil 400 mg/m2, doxorubicin 40 mg/m2, cyclophosphamide 400 mg/m2, full dose | N/A                                         | metastatic cancer, rapidly growing tumors, pretreatment high LDH, and high tumor burden |
| Meeks, 2016 [91] | 46  | M      | unknown primary cancer | Steroid: dexamethasone 4 mg per 6 hours, full dose | 2 days after initiation | anemia, lower back pain                                                  | metastatic cancer and bulky tumor                                       |
| Busam, 2004 [92] | 36  | F      | melanoma             | bio-chemo therapy: cisplatin, vinblastine, dacarbazine, interferon-α, interleukin-2 | N/A                                         | metastatic cancer                                                        |}

**Notes:**
- DM: diarrhea
- SOB: shortness of breath
- HCC: hepatocellular carcinoma
- N/A: not available
- High LDH: high levels of lactate dehydrogenase
- Metastatic cancer: cancer that has spread beyond the original site of the tumor
- Bulky tumor: tumor that is large and can cause pressure on surrounding tissues or organs
- Customized treatments and management strategies are described as per the respective studies.
| Reference | Age | Gender | Diagnosis  | Treatment | Onset | Symptoms | Complications |
|-----------|-----|--------|------------|-----------|-------|----------|---------------|
| Michels, 2010 | 70 | M | HCC | Targeted therapy: sunitinib 50 mg daily for 4 weeks | Day 18 after initiation of treatment | N/A | fever, headache, vomiting | bulky tumor and metastatic tumor |
| Nakamura, 2009 | 48 | M | RCC | Chemotherapy: cisplatin 70mg/m², full dose | N/A | N/A | weakness and malaise | metastatic tumor and bulky |
| Gouveia, 2018 | 51 | F | colorectal cancer | Palliative chemotherapy: oxaliplatin 85 mg/m², 5-fluorouracil 400 mg/m² bolus, 2400 mg/m² continuous infusion, full dose | after completing three cycles | HTN, obesity | asthenia, giddiness, fine tremor | metastatic tumor; pretreatment high LDH |
| Huang, 2009 | 55 | M | HCC | Targeted therapy: sorafenib 400 mg twice every day, full dose | 30 days after sorafenib started | Hepatitis B | jaundice, oliguria, weakness | N/A |
| Lin, 2007 | 72 | M | prostate carcinoma | Spontaneous | N/A | N/A | anorexia, fatigue, and severe pedal edema | metastatic tumor |
| Nicholasou, 2007 | 67 | F | RCC | Targeted therapy: sunitinib | between days 3-9 of treatment | N/A | watery stools, nausea, vomiting, and fatigue | metastatic tumor |
| Norberg, 2014 | 56 | M | RCC | Spontaneous | N/A | HTN | severe back pain, night sweats, weight loss and low-grade fevers | metastatic tumor |
| Oztolci, 2004 | 66 | M | colon cancer | Chemotherapy: irinotecan 180 mg/m² 5-fluorouracil 400 mg/m² bolus 600 mg/m² continuous infusion leucovorin 200mg/m², full dose | 1 cycle: 72 hours after initiation | N/A | oliguria | metastatic tumor |
| Pabon, 2018 | Mid age | F | uterine leiomyosarcoma | Chemotherapy: rubin mesylate 1.4mg/m², full dose | cycle 1 : day 8 after initiation | N/A | fatigue, dyspnoea, and poor appetite | metastatic tumor and bulky tumor |
| Pindak, 2019 | 19 | M | testicular germ cell tumor | Surgery: radical resection of the tumor | during the surgery | N/A | cardiac arrhythmia | bulky tumor and metastatic tumor |
| Rostom, 2000 | 73 | M | breast cancer | Radiotherapy: upper hemi-body radiation (UHBr) total breast dose 9.65 Gy, full dose | 48 hours after initiation | DM | drowsy, confused | metastatic tumor |
| Romo, 2019 | 28 | M | oligodendroglioma | Radiotherapy: IMRT with a cumulative dose of 5940 cGy over 33 fractions | N/A | N/A | N/A | metastatic tumor and rapidly growing tumor |
| Okay, 2019 | 61 | M | HCC | Chemotherapy: TACE (ethanol and lipiodol) | 2 weeks after initiation | Chronic myeloid leukemia | N/A | N/A |
| Dhakal, 2018 | 70 | M | small cell neuroendocrine carcinoma | Spontaneous | N/A | Coronary artery disease | N/A | N/A |

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| Name, Year | Age | Gender | Diagnosis/Condition | Initial Therapy | Duration | Metastatic/Deterioration
|------------|-----|--------|---------------------|----------------|----------|-------------------------|
| Shozawa, 2010 [108] | 79 | F | HCC | targeted therapy: sorafenib | 1 cycle: 10 days after initiation | hepatitis C and liver cirrhosis | N/A | N/A | bulky and metastatic tumor, highly sensitive to chemotherapy, and pretreatment high LDH |
| Dirix, 1991 [109] | 65 | F | Merkel cell carcinoma | chemotherapy: doxorubicin 50mg/m2 IV bolus, and 5 g/m2 continuous infusion over 24 hours of ifosfamide, full dose | 1 cycle: 4 days after chemotherapy initiation | N/A | anuria. | |
| Shamseddine, 1993 [110] | 66 | F | Valvular cancer | chemotherapy: cisplatin, 50 mg as continuous infusion over 4 hours daily for 3 days, 5 FU, 1500 mg as continuous infusion over 24 hours for 5 days, full dose. | 1 cycle | N/A | tachypnea and sweating | bulky and metastatic tumor |
| Song, 2011 [111] | 46 | M | Melanoma | spontaneous | N/A | N/A | abdominal pain, nausea, vomiting, and dyspnea |
| Takeuchi, 2016 [112] | 62 | M | Melanoma | spontaneous | N/A | DM | oliguria and back pain |
| Kim, 2014 [113] | 59 | M | Colon cancer | chemotherapy: 5-FU, leucovorin, and oxaliplatin | 2nd cycle: 3 days after chemotherapy initiation, and 3rd cycle: 3 days after chemotherapy. | N/A | N/A | metastatic tumor |
| Chow, 2015 [114] | 47 | M | Testicular cancer | hormonal therapy: tamoxifen 10mg by mouth twice a day, full dose | one week after initiation | N/A | breathlessness, bilateral limb swelling, and tachypnea. | N/A |
| Cech, 1986 [115] | 94 | F | Breast cancer | hormonal therapy: tamoxifen 10mg by mouth twice a day, full dose | N/A | N/A | bone pain | metastatic cancer |
| Feld, 2000 [116] | 72 | M | Lung adenocarcinoma | spontaneous | N/A | N/A | increasing abdominal girth, jaundice, fever, weight lose, and night sweats | high baseline LDH and metastatic |
| Boisseau, 1996 [117] | 42 | F | Colon cancer | Chemotherapy: irinotecan 300mg/m2, reduced dose | 8 days after initiation | N/A | general deterioration | metastatic, bulky, and rapid growth tumor |
| Alaigh, 2017 [118] | 58 | F | Leiomyosarcoma | spontaneous | N/A | N/A | abdominal distention, constipation, nausea, fatigue, and SOB | metastatic |
| Pinder, 2007 [119] | 81 | M | Gastrointestinal stromal tumor (GIST) | target therapy: imatinib 400mg once daily, full dose | 2 days after initiation | N/A | SOB, oedema, and poor urine output | metastatic and bulky tumor |
| Author, Year     | Age | Gender | Primary Diagnosis                  | Treatment Type                                                                 | Onset Duration | Symptoms                                                                                     | Additional Notes                                                                 |
|------------------|-----|--------|------------------------------------|--------------------------------------------------------------------------------|----------------|---------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Kurt, 2005       | 52  | M      | lung adenocarcinoma                | bone modifying therapy: zoledronic acid IV infused within 15 minutes          | 4 days         | N/A                                                                                         | metastatic, bulky and large tumor border                                         |
| Kawai, 2006      | 26  | M      | testicular cancer                  | chemotherapy: bleomycin, etoposide and cisplatin (BEP)                      | 1 day          | N/A                                                                                         | metastatic and pretreatment high LDH                                              |
| Vaisban, 2003    | 82  | F      | colon cancer                       | spontaneous                                                                  | N/A            | weakness, oliguria, and confusion                                                           | metastatic tumor                                                                |
| Vaisban, 2003    | 80  | M      | pheochromocytoma                   | spontaneous                                                                  | N/A            | abdominal pain, fever, and vomiting                                                         | N/A                                                                              |
| Vaisban, 2003    | 72  | M      | HCC                                | spontaneous                                                                  | N/A            | abdominal pain, dyspnea, and weakness                                                       | N/A                                                                              |
| Okamoto, 2015    | 62  | F      | ovarian cancer                     | spontaneous                                                                  | N/A            | lower abdominal pain, back pain, and anuria                                                  | bulky                                                                           |
| Boyd, 2017       | 56  | M      | prostate cancer                    | chemotherapy: oxaliplatin, docetaxel, 5-fluorouracil, and leucovorin         | N/A            | N/A                                                                                         | abdominal pain                                                                  |
| Vodopivec, 2012  | 57  | M      | gastric adenocarcinoma             | chemotherapy: oxaliplatin, docetaxel, 5-fluorouracil, and leucovorin         | 7 days         | Nausea, vomiting, oliguria, and generalized weakness                                          | metastatic                                                                      |
| Tseng, 2016      | 65  | M      | colon cancer                       | chemotherapy: oxaliplatin 160 mg, 5-fluorouracil 2800 mg (1500 mg/m2) for 1 day | 1st cycle      | chest tightness, altered level of consciousness, and ventricular tachycardia                 | metastatic tumor                                                                |
| Berringer, 2017  | 48  | M      | colon cancer                       | spontaneous                                                                  | N/A            | abdominal pain, jaundice, weakness, and anorexia                                             | metastatic tumor and large tumor burden                                         |
| Sommerhalder, 2017 | 49  | F      | colon cancer                       | spontaneous                                                                  | N/A            | edema of bilateral extremities associated with worsening dyspnea                               | metastatic tumor                                                                |
| Shenoy, 2009     | 74  | M      | SCLC                               | spontaneous                                                                  | N/A            | COPD, coronary artery disease, and HTN                                                        | anuria, lethargy, and weakness                                                 |
| Lee, 2013        | 40  | F      | thymoma                            | chemotherapy: IV paclitaxel 175mg/m2, IV ifosfamide 2500mg/m2, full dose     | second day     | tachypnea, tachycardia, and oliguria                                                        | bulky, pretreatment high LDH, and metastatic tumor                              |
| Tanvetyanon, 2004 | 77  | M      | prostate cancer                    | hormonal therapy: goserelin acetate 10.8mg, full dose                        | 6 days         | Lethargic and flapping tremor                                                              | bulky, pretreatment high LDH, and metastatic tumor                              |
| Ustundag, 1997   | 56  | F      | breast cancer                      | chemotherapy: paclitaxel IV infusion for 24 hours, full dose                | one day        | orthopnea, oliguria, and anuria                                                            | Metastatic cancer, high pretreatment LDH                                      |
| Authors          | Year | Age | Sex | Diagnosis                  | Treatment Details                                                                 | Time to onset | Associated Symptoms | Description                                                                 |
|------------------|------|-----|-----|----------------------------|-----------------------------------------------------------------------------------|---------------|---------------------|----------------------------------------------------------------------------|
| Abbouda, 2009    | 53   | M   | maxillary sinus cancer     | adjuvant chemoradiation: 66 Gy to the tumor bed and 50 Gy to the upper neck area, full dose | 4 days after initiation | N/A           | decreased level of consciousness and abdominal pain. | metastatic cancer |
| Barton, 1989     | 57   | F   | breast cancer              | chemotherapy: cyclophosphamid e 500mg/m2, methotrexate 30mg/m2 and 5-fluorouracil 500mg/m2, full dose | 1 day after initiation | N/A           | dyspnea             | bulky, metastatic tumor, pretreatment high LDH, rapid tumor growth, and large tumor border |
| Barton, 1989     | 58   | M   | seminoma                   | chemotherapy: vinblastine 0.2 mg/kg/d and IV bleomycin 30 units daily, full dose | 2 days after initiation | N/A           | N/A                 | bulky, metastatic tumor, pretreatment high LDH, rapid tumor growth, and large tumor border |
| Mott, 2005       | 47   | F   | breast cancer              | chemotherapy: fluorouracil/epirubicin/cyclophosphamide, full dose | 1 day after initiation | N/A           | lethargy and lightheadedness | metastatic cancer |
| Mott, 2005       | 44   | F   | breast cancer              | chemotherapy: gemcitabine and cisplatin, full dose | 1 day after initiation | N/A           | nausea, dizziness, and decreased oral intake | metastatic cancer |
| Mott, 2005       | 76   | F   | SCLC                        | chemotherapy: carboplatin and etoposide full dose | 4 days after initiation | N/A           | nausea and dehydration | metastatic cancer and high pretreatment LDH |
| Qian, 2009       | 44   | M   | primary retroperitoneal soft tissue sarcoma | chemotherapy: cisplatin 30 mg/m2 intravenously on days 1 through 4, doxorubicin 30 mg/m2 intravenously on days 1 and 3, dacarbazine 400 mg/m2 intravenously on days 1 through 3, full dose | 3 days after initiation | N/A           | drowsiness, chest tightness, palpitations, dyspnea, and oliguria | metastatic cancer and chemosensitivity |
| Yuan, 2017       | 43   | M   | GIST                        | targeted therapy: Imatinib 400mg, full dose | 1 day after initiation | N/A           | loss of consciousness | high tumor border and metastatic tumor |
| Lin, 2007        | 75   | F   | RCC                         | chemotherapy: gemcitabine monotherapy at a dosage of 1200 mg/m2 as a 30 minutes intravenous infusion, full dose | 2 weeks after initiation | CKD           | anorexia, fatigue, pedal edema, dyspnea, and anuria | metastatic cancer |
| Ling, 2012       | 40   | M   | pancreatic cancer           | Chemotherapy: gemcitabine | 2 days after initiation | N/A           | nausea and vomiting | metastatic cancer |
| Sharma, 2006     | 63   | M   | HCC                         | chemotherapy: TACE (fluourouracil 1gm, Cisplatin 80mg, mitomycin 20mg and lipiodol | 1 day after initiation | hepatitis B | fever, nausea, and oliguria | metastatic cancer |
Additional Information

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following.

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TABLE 8: Characteristics of included studies

| HCC: hepatocellular carcinoma | TACE: trans arterial chemoembolisation | HTN: hypertension | DM: diabetes mellitus | CKD: chronic kidney disease | LDH: lactate dehydrogenase | RCC: renal cell carcinoma | NSCLC: non-small cell lung cancer | COPD: chronic obstructive pulmonary disease | SCLC: small cell lung cancer | PVE: portal vein embolisation | ESOS: extraskelletal osteosarcoma | SOB: shortness of breath | BAC: bronchialalveolar carcinoma | TLS: tumor lysis syndrome |
|------------------------------|--------------------------------------|-----------------|-------------------|-----------------|-------------------------|-------------------------|-----------------|-----------------|------------------|-----------------|-----------------|-------------------|-----------------|------------------|-------------------|
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