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Pomalidomide

Updated: August 30, 2022.

OVERVIEW

Introduction

Pomalidomide is an immunomodulatory and antineoplastic agent that is used in the therapy of multiple myeloma. Pomalidomide, like the structurally related agents thalidomide and lenalidomide, is associated with a low rate of serum aminotransferase elevations during therapy and has been implicated in causing rare instances of clinically apparent liver injury which can be severe.

Background

Pomalidomide (pom" a lid' oh mide) is a thalidomide derivative (3-amino-thalidomide) similar to lenalidomide that has potent immunomodulatory and antiangiogenic activity and is used as an antineoplastic agent. The mechanism of action of these agents in the treatment of multiple myeloma is not well defined but may relate to inhibition of tumor necrosis factor (TNF) alpha, a potent proinflammatory cytokine or to stimulation of T and NK cell activity. In vitro and in animal models, pomalidomide had greater antineoplastic activity and was less toxic than thalidomide and lenalidomide, but direct comparisons of these agents in humans have not been done. Pomalidomide was approved for use (combined with dexamethasone) in the United States for refractory multiple myeloma in 2015. It subsequently was given accelerated approval as therapy of Kaposi sarcoma. Pomalidomide has also been used on an experimental basis for myelofibrosis and other myeloproliferative disorders. Pomalidomide is available in capsules of 1, 2, 3 and 4 mg under the brand name Pomalyst. The recommended dose for multiple myeloma is 4 mg daily for 21 days in cycles of 28 days indefinitely or until there is disease progression or intolerance. The dose in Kaposi sarcoma is 5 mg daily for 21 days in cycles of 28 days. Its use is restricted because of teratogenicity and strict adherence to birth control (for both men and women) is required. Side effects of pomalidomide are common and similar to those of thalidomide and lenalidomide and include sedation, dizziness, orthostatic hypotension, neutropenia, thrombocytopenia, anemia, peripheral neuropathy and arterial and venous thromboembolism (for which reason it is usually given with antiplatelet agents such as aspirin or with anticoagulation). Rare but potentially severe adverse events include severe cutaneous reactions, severe neuropathy, secondary malignancies, tumor lysis syndrome and hypersensitivity reactions. Pomalidomide is a teratogen and possible cause of severe birth defects and is available only as a part of a strict Risk Evaluation and Mitigation Strategy (REMS), which requires physician training, written patient informed consent, strict birth control measures, regular monitoring and reporting.

Hepatotoxicity

Serum enzyme elevations occur in 1% to 2% of patients taking pomalidomide and are more frequent with higher doses. The enzyme abnormalities are usually mild and self-limited and rarely require drug discontinuation. In

addition pomalidomide has been implicated in rare instances of clinically apparent, acute liver injury which can be severe and has been reported to lead to deaths from acute liver failure. However, few of these cases have been published and the clinical features, course and outcome of the typical case of liver injury from pomalidomide have not been defined. Both thalidomide and lenalidomide have been implicated in cases of clinically apparent acute liver injury and the presentation and course of injury is likely to be similar to that caused by pomalidomide. The latency to onset of cases of thalidomide associated liver injury is usually within 1 to 6 weeks of starting the antineoplastic agent. The clinical features vary greatly and can be hepatocellular or cholestatic. Cases of acute liver failure as well as vanishing bile duct syndrome with rapid marked cholestasis and hepatic failure have been described with thalidomide and lenalidomide. Immunoallergic features may be prominent and instances of Stevens Johnson syndrome and toxic epidermal necrolysis with and without liver injury have also been linked to therapy with thalidomide and its derivatives. In most cases, the injury resolves rapidly after therapy is stopped. Monitoring of liver tests at monthly intervals is recommended when using thalidomide and its derivatives, and stopping therapy early may play an important role in preventing severe and fatal outcomes.

Pomalidomide and the thalidomide derivatives have also been implicated in causing an increased risk of graft-vs-host disease after autologous or allogeneic hematopoietic stem cell transplantation (HSCT) as well as after liver, kidney and heart transplantation. There appears to be cross reactivity to this complication among lenalidomide, pomalidomide and thalidomide. Therapy usually requires discontinuation of the antineoplastic agent as well as treatment with high doses of corticosteroids and tacrolimus or sirolimus. Furthermore, hepatic graft-vs-host disease can occasionally present with an acute hepatitis that resembles hepatocellular drug induced liver injury.

Reactivation of hepatitis B has been reported in patients receiving thalidomide, lenalidomide and pomalidomide, but generally only after HSCT and the role of these agents in causing reactivation is not always clear. Indeed, in studies of large numbers of patients treated for multiple myeloma the major risk factor for hepatitis B reactivation was found to be HSCT rather than the specific antineoplastic drugs being used. Indeed, lenalidomide therapy is associated with a reduced risk of reactivation in patients with HSCT (although dexamethasone, thalidomide and bortezomib were not), perhaps because of the immune enhancement typically caused by lenalidomide.

Likelihood score: D (possible cause of clinically apparent liver injury).

Mechanism of Injury

The mechanism of pomalidomide hepatotoxicity is not clear, but it may be related to its activity in reducing TNF-α production, a potent inflammatory cytokine that activates T cells and promotes inflammation, but is also necessary for normal liver regeneration. Alternatively, the injury may be triggered by an intermediate of its metabolism, which is largely mediated by hepatic microsomal enzymes, CYP 1A2 and 3A4.

Outcome and Management

The severity of pomalidomide induced liver injury ranges from transient, asymptomatic elevations in serum enzymes to acute liver injury with jaundice to severe acute liver failure and death. Vanishing bile duct syndrome has been reported with use of thalidomide and lenalidomide but not specifically with pomalidomide. Regular monitoring of liver tests is recommended during pomalidomide therapy. Patients who develop liver test abnormalities should stop therapy and restart treatment only if the abnormalities are transient and not associated with symptoms or jaundice. While not proven, the various thalidomide derivatives are likely to demonstrate cross sensitivity to clinically apparent liver injury.

Drug Class: Antineoplastic Agents, Miscellaneous

Other Related Drugs: Lenalidomide, Thalidomide

CASE REPORT

Case 1. Acute liver injury with jaundice due to pomalidomide.(1)

A 47 year old African American man with refractory multiple myeloma, who had received multiple courses of therapy and an allogenic hematopoietic cell transplant, developed nausea and rash 3 weeks into a first course of pomalidomide (2 mg daily for 21 days) and dexamethasone (20 mg weekly). Shortly thereafter he was found to be jaundiced and was admitted for evaluation and management. He had no history of liver disease, alcohol abuse or risk factors for viral hepatitis. He had had several bouts of graft-vs-host disease after the hematopoietic cell transplant which had been managed with immunosuppression and extracorporeal photopheresis. On hospital admission, total bilirubin was 16.2 mg/dL (direct 12 mg/dL), ALT 1241 U/L, AST 552 U/L, alkaline phosphatase (Alk P) 337 U/L. The prothrombin time was 22.8 seconds. Tests for hepatitis A, B and C and for EBV and CMV infection were negative. A CT of the abdomen showed no evidence of biliary obstruction. A liver biopsy showed severe hepatocyte necrosis and portal inflammation with lymphocytes, plasma cells and eosinophils. The bile ducts showed reactive changes but no inflammation or loss, and hepatic arteries and veins were normal without endothelitis. The biopsy was considered compatible with severe drug induced liver injury and not suggestive of acute or chronic graft-vs-host disease. Over the next few weeks, liver tests improved and liver tests were only mildly abnormal when he was seen as an outpatient two weeks later.

Key Points

Medication:	Pomalidomide (2 mg daily)
Pattern:	Hepatocellular (R ratio=12.4)
Severity:	4+ (jaundice, hospitalization, coagulopathy)
Latency:	3 weeks
Recovery:	Marked improvement within 2 weeks
Other medications:	None mentioned, except for dexamethasone.

Laboratory Values

Time After Starting	Time After Stopping	ALT* (U/L)	Alk P* (U/L)	Bilirubin* (mg/dL)	Other
3 weeks	0	Symptoms of increasing nausea and rash			
4 weeks	~6 days	1241	337	16.2	Admission
	8 days	900	280	14.0	
	9 days	820	340	18.4	
	10 days	640	400	17.4	
5 weeks	11 days	560	380	14.2	Discharge
6 weeks	19 days	80	200	4.4	
Normal Values**		**<40**	**<135**	**<1.2**	

* Most values estimated from Figure 1.
** Normal values not provided, these being standard levels

Comment

This man with advanced refractory multiple myeloma, who had received autologous followed by an allogenic hematopoietic cell transplants, developed jaundice approximately 3 weeks after starting a new chemotherapy

regimen of pomalidomide and dexamethasone. The jaundice was initially thought to be due to graft-vs-host disease, but a liver biopsy was more compatible with a severe, acute drug induced hepatocellular injury. Other causes of acute liver injury were appropriately excluded. The time to onset, pattern of serum enzyme elevations, history of preexisting liver disease (graft-vs-host liver injury) and rapid improvement with stopping the implicated agent all resemble the features of drug induced liver injury from thalidomide and lenalidomide. It is not known whether there is cross sensitivity to liver injury among the different thalidomide derivatives. Interestingly, he had previously received thalidomide, evidently without liver injury, so that this episode might represent a reexposure.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Pomalidomide – Pomalyst®

DRUG CLASS

Antineoplastic Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULAS AND STRUCTURES

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Thalidomide	50-35-1	C13-H10-N2-O4	SID: 134971183
Lenalidomide	191732-72-6	C13-H13-N3-O3	SID: 135134887
Pomalidomide	19171-19-8	C13-H11-N3-O4	SID: 135089995

CITED REFERENCES

1. Pauff JM, Gonzalez RS, Sajnani KP, Kassim A, Jagasia M. Post-allograft pomalidomide and reversible hepatotoxicity. Bone Marrow Transplant. 2014;49:1341–2. PubMed PMID: 24955783.

ANNOTATED BIBLIOGRAPHY

References updated: 30 August 2022

Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999.

(Textbook of hepatotoxicity published in 1999; thalidomide and pomalidomide are not discussed).

Davern TJ. Hepatotoxicity of immunomodulating agents and the transplant situation. Thalidomide. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 2nd ed. New York: Informa Healthcare USA, 2007, p. 675.

(Mentions that thalidomide rarely causes liver injury, but case reports of hepatocellular injury with variable degrees of jaundice have been described, largely in patients with preexisting chronic liver disease).

Wellstein A, Giaccone G, Atkins MB, Sausville EA. Thalidomide and Lenalidomide. Pathway targeted therapies: monoclonal antibodies, protein kinase inhibitors, and various small molecules. In, Brunton LL, Hilal-Dandan R, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 13th ed. New York: McGraw-Hill, 2018, pp. 1225-27.

(Textbook of pharmacology and therapeutics).

Clark TE, Edom N, Larson J, Lindsey LJ. Thalomid (Thalidomide) capsules: a review of the first 18 months of spontaneous postmarketing adverse event surveillance, including off-label prescribing. Drug Saf. 2001;24:87–117. PubMed PMID: 11235821.

(During first 18 months of postmarketing use of thalidomide in 10,456 patients, 1210 adverse event reports were received, including 4 cases of hepatic failure arising after 1-4 weeks of treatment, although 3 were considered unrelated to therapy).

Fowler R, Imrie K. Thalidomide-associated hepatitis: a case report. Am J Hematol. 2001;66:300–2. PubMed PMID: 11279644.

(Patient with chronic hepatitis C and advanced plasma cell leukemia developed jaundice and nausea 1 week after starting thalidomide [bilirubin 0.4 initially rising to 9.3 mg/dL, ALT 91 to 829 U/L, Alk P 100 to 120 U/L], resolving rapidly upon stopping; high HCV RNA levels noted).

Trojan A, Chasse E, Gay B, Pichert G, Taverna C. Severe hepatic toxicity due to thalidomide in relapsed multiple myeloma. Ann Oncol. 2003;14:501–2. PubMed PMID: 12598363.

(62 year old woman with multiple myeloma developed acute liver failure after 7 months of thalidomide therapy [bilirubin not given, ALT ~2000 U/L, LDH ~6000 U/L], enzymes falling to normal in 1 week; overall, suggestive of ischemic hepatitis rather than drug induced liver injury).

Teo SK. Properties of thalidomide and its analogues: implications for anticancer therapy. AAPS J. 2005;7:E14–E19. PubMed PMID: 16146335.

(Review of the properties and experimental uses of thalidomide as an inhibitor of TNF-α and other cytokines in multiple myeloma and several solid tumors).

Hanje AJ, Shamp JL, Thomas FB, Meis GM. Thalidomide-induced severe hepatotoxicity. Pharmacotherapy. 2006;26:1018–22. PubMed PMID: 16803426.

(Elderly woman with multiple myeloma developed jaundice and marked ALT elevations 6 weeks after starting thalidomide [ALT 2205 U/L; bilirubin 5.6 mg/dL], resolving within 3 months of stopping: Case 1 for Thalidomide).

Hamadani M, Benson DM Jr, Copelan EA. Thalidomide-induced fulminant hepatic failure. Mayo Clin Proc. 2007;82:638.

(64 year old woman with multiple myeloma and HBsAg in serum developed acute liver failure 12 days after starting thalidomide [bilirubin 16.7 mg/dL, ALT 410 U/L, Alk P 101 U/L, no change in HBV DNA], some improvement on stopping drug, but had worsening coagulopathy and renal failure and died 14 days later).

Melchert M, List A. The thalidomide saga. Int J Biochem Cell Biol. 2007;39:1489–99. PubMed PMID: 17369076.

(Review of history of thalidomide and current understanding of its actions as an anticytokine; no mention of side effects).

Hussain S, Browne R, Chen J, Parekh S. Lenalidomide-induced severe hepatotoxicity. Blood. 2007;110:3814. PubMed PMID: 17984315.

(57 year old man with multiple myeloma developed jaundice 1 week after starting lenalidomide, a derivative of thalidomide [bilirubin 7.2 mg/dL, ALT 90 U/L, Alk P 210 U/L], resolving within 3 weeks).

Dabak V, Kuriakose P. Thalidomide-induced severe hepatotoxicity. Cancer Chemother Pharmacol. 2009;63:583–5. PubMed PMID: 19083237.

(2 women with multiple myeloma; 79 year old developed jaundice 7 weeks after starting thalidomide [bilirubin 27.9 mg/dL, ALT 392 U/L, Alk P 1172 U/L], with persistent jaundice, bile duct loss on liver biopsy and death 4 months later; 57 year old developed raised enzymes one month after starting thalidomide [bilirubin not given, ALT 398 U/L, Alk P 175 U/L], resolving within 2 weeks of stopping).

Levesque E, Bradette M. Hepatotoxicity as a rare but serious side effect of thalidomide. Ann Hematol. 2009;88:183–4. PubMed PMID: 18665361.

(36 year old woman with multiple myeloma developed liver test abnormalities 5 weeks after starting thalidomide [bilirubin normal, peak ALT ~1300 U/L], resolving within 20 days of stopping).

Jain P. Lenalidomide-induced acute liver failure. Blood Transfus. 2009;7:335–6. PubMed PMID: 20011646.

(93 year old man with myelodysplastic syndrome and HBsAg in serum developed jaundice 10 days after starting lenalidomide [bilirubin 9.2 mg/dL, ALT 2670 U/L, Alk P 342 U/L, IgM anti-HBc positive, but HBV DNA negative], resolving over following 4 weeks; patient later tolerated restarting lenalidomide in combination with adefovir).

Castaneda CP, Brandenburg NA, Bwire R, Burton GH, Zeldis JB. Erythema multiforme/Stevens-Johnson syndrome/toxic epidermal necrolysis in lenalidomide-treated patients. J Clin Oncol. 2009;27:156–7. PubMed PMID: 19047275.

(After approximately 57,000 patients had received lenalidomide, the sponsor received 12 reports of Stevens-Johnson Syndrome, 3 of erythema multiforme and 1 of toxic epidermal necrolysis, arising 3-112 days after starting; often sparse data were available and there was no mention of liver injury or jaundice).

Tefferi A, Verstovsek S, Barosi G, Passamonti F, Roboz GJ, Gisslinger H, Paquette RL, et al. Pomalidomide is active in the treatment of anemia associated with myelofibrosis. J Clin Oncol. 2009;27:4563–9. PubMed PMID: 19652059.

(Among 84 patients with anemia due to myelofibrosis who were treated with pomalidomide [0.5 or 2 mg daily] with or without prednisone or prednisone alone, side effects were largely due to myelosuppression and venous thromboses [5%]; no mention of ALT elevations or hepatotoxicity).

Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. Hepatology. 2010;52:2065–76. PubMed PMID: 20949552.

(Among 1198 patients with acute liver failure enrolled in a US prospective study between 1998 and 2007, 133 were attributed to drug induced liver injury, but none were attributed to thalidomide or its derivatives).

Begna KH, Mesa RA, Pardanani A, Hogan WJ, Litzow MR, McClure RF, Tefferi A. A phase-2 trial of low-dose pomalidomide in myelofibrosis. Leukemia. 2011;25:301–4. PubMed PMID: 21052089.

(Among 58 patients with myelofibrosis treated with low doses of pomalidomide [0.5 mg daily], anemia responses occurred in 10 subjects [16%]; side effects were said to be less than with standard doses; no mention of ALT elevations or hepatotoxicity).

Zanella MC, Rubbia-Brandt L, Giostra E, Chalandon Y, Hadengue A, Spahr L. A case of drug-induced hepatitis due to lenalidomide. Case Rep Gastroenterol. 2011;5:217–22. PubMed PMID: 21552449.

(50 year old man developed severe skin rash 3 months after starting lenalidomide that resolved upon stopping, but developed serum enzyme elevations one week after restarting lenalidomide 2 years later [bilirubin normal, ALT 509 U/L, Alk P 198 U/L], resolving upon stopping).

Vilas-Boas F, Gonçalves R, Sobrinho Simões M, Lopes J, Macedo G. Thalidomide-induced acute cholestatic hepatitis: case report and review of the literature. Gastroenterol Hepatol. 2012;35:560–6. PubMed PMID: 22789729.

(77 year old man with multiple myeloma developed jaundice 4 weeks after starting chemotherapy with melphalan, prednisone and thalidomide [bilirubin 11.4 mg/dL, ALT 333 U/L, Alk P 4 times ULN], worsening for a week after stopping thalidomide and then improving; patient later tolerated melphalan but died of pneumonia shortly thereafter).

Nojkov B, Signori C, Konda A, Fontana RJ. Lenalidomide-associated hepatotoxicity--a case report and literature review. Anticancer Res. 2012;32:4117–9. PubMed PMID: 22993370.

(67 year old man with multiple myeloma developed fatigue within 1 week of starting a 2nd 3-week course of lenalidomide [bilirubin 4.4 mg/dL, ALT 139 U/L, Alk P 190 U/L], with rapid resolution upon stopping [within 8 days]).

Richardson PG, Siegel D, Baz R, Kelley SL, Munshi NC, Laubach J, Sullivan D, et al. Phase 1 study of pomalidomide MTD, safety, and efficacy in patients with refractory multiple myeloma who have received lenalidomide and bortezomib. Blood. 2013;121:1961–7. PubMed PMID: 23243282.

(Among 38 patients with refractory multiple myeloma treated with pomalidomide [2-5 mg daily for 21 days in 28 day cycles], dose limiting toxicities were uncommon; no mention of ALT elevations or hepatotoxicity).

Leleu X, Attal M, Arnulf B, Moreau P, Traulle C, Marit G, Mathiot C, et al. Pomalidomide plus low-dose dexamethasone is active and well tolerated in bortezomib and lenalidomide-refractory multiple myeloma: Intergroupe Francophone du Myélome 2009-02. Blood. 2013;121:1968–75. PubMed PMID: 23319574.

(Among 84 patients with refractory multiple myeloma treated with pomalidomide in 28 day courses, the 1 year relapse-free survival rate was 44%; all patients had adverse events which were usually hematologic; no mention of ALT elevations or hepatotoxicity).

Lacy MQ, McCurdy AR. Pomalidomide. Blood. 2013;122:2305–9. PubMed PMID: 23974193.

(Review of safety and efficacy of pomalidomide which the authors claim has a lower rate of hematologic toxicities than thalidomide and lenalidomide; no mention of ALT elevations or hepatotoxicity).

Björnsson ES, Bergmann OM, Björnsson HK, Kvaran RB, Olafsson S. Incidence, Presentation and Outcomes in Patients with Drug-Induced Liver Injury in the General Population of Iceland. Gastroenterology. 2013;144:1419–25. PubMed PMID: 23419359.

(In a population based study of drug induced liver injury from Iceland, 96 cases were identified over a 2 year period, but none were attributed to thalidomide or its derivatives).

Richardson PG, Siegel DS, Vij R, Hofmeister CC, Baz R, Jagannath S, Chen C, et al. Pomalidomide alone or in combination with low-dose dexamethasone in relapsed and refractory multiple myeloma: a randomized phase 2 study. Blood. 2014;123:1826–32. PubMed PMID: 24421329.

(Among 221 patients with refractory multiple myeloma treated with pomalidomide with or without dexamethasone, median progression free survival was 2.6 months with pomalidomide alone and 4.6 months with addition of dexamethasone; adverse events included neutropenia, anemia, thrombocytopenia, pneumonia and fatigue; no mention of ALT elevations or hepatotoxicity).

Pauff JM, Gonzalez RS, Sajnani KP, Kassim A, Jagasia M. Post-allograft pomalidomide and reversible hepatotoxicity. Bone Marrow Transplant. 2014;49:1341–2. PubMed PMID: 24955783.

(47 year old man with recurrence of multiple myeloma after hematopoietic cell transplant developed jaundice three weeks after starting pomalidomide [2 mg daily] and dexamethasone [bilirubin 16.2 mg/dL, ALT 1241 U/L, Alk

P 337 U/L, protime 22.8 sec], biopsy showing marked necrosis without evidence of GvHD, liver test improving rapidly within the next 2 weeks: Case 1).

Veluswamy RR, Ward SC, Yum K, Abramovitz RB, Isola LM, Jagannath S, Parekh S. Adverse drug reaction: pomalidomide-induced liver injury. Lancet. 2014;383(9935):2125–6.

(50 year old man with refractory, relapsed multiple myeloma and both autologous and allogeneic hematopoietic stem cell transplant developed serum ALT elevations after starting pomalidomide, which progressed to acute liver injury despite dose reduction [bilirubin 13.1 mg/dL, ALT 3981 U/L, Alk P 259 U/L] that improved on stopping and high dose prednisone but then worsened and liver biopsy suggested acute graft-vs-host disease, which responded to restarting prednisone and adding sirolimus).

Hernández N, Bessone F, Sánchez A, di Pace M, Brahm J, Zapata R, A, Chirino R, et al. Profile of idiosyncratic drug induced liver injury in Latin America: an analysis of published reports. Ann Hepatol. 2014;13:231–9. PubMed PMID: 24552865.

(Among 176 reports of drug induced liver injury from Latin America published between 1996 and 2012, none were attributed to thalidomide or its derivatives).

Pomalidomide (Pomalyst) for multiple myeloma. Med Lett Drugs Ther. 2015;57:e66–7.

(Concise review of the mechanism of action, efficacy, safety and costs of pomalidomide shortly after its approval for use in the US mentions adverse side effects of neutropenia, thrombocytopenia, venous thromboses, tumor lysis syndrome, dizziness, confusion, neuropathy and acute lung toxicity; no mention of ALT elevations or hepatotoxicity).

Modi D, Mamdani H, Vettese T. Pomalidomide-Induced pulmonary toxicity in multiple myeloma. Am J Med Sci. 2015;350:241–2. PubMed PMID: 26200951.

(69 year old man with multiple myeloma developed pneumonitis [dyspnea, hypoxia, pulmonary opacities] 8 months after starting pomalidomide, resolving rapidly on stopping, recurring on reexposure, then resolving with corticosteroid therapy; no mention of liver test abnormalities).

Chalasani N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, Reddy KR, et al; United States Drug Induced Liver Injury Network. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN Prospective Study. Gastroenterology. 2015;148:1340–52.e7. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, 1 case was attributed to thalidomide, none to lenalidomide or pomalidomide).

Danhof S, Schreder M, Strifler S, Einsele H, Knop S. Long-term disease control by pomalidomide/dexamethasone-based therapy in a patient with advanced multiple myeloma: a case report and review of the literature. Case Rep Oncol. 2015;8:189–95. PubMed PMID: 25969681.

(59 year old woman with multiple myeloma underwent multiple courses of chemotherapy over a 9 year period and finally with pomalidomide, dexamethasone and doxorubicin had a partial response but developed reactivation of hepatitis B after 6 cycles [HBV DNA 10^7 copies/mL], which was controlled by entecavir allowing for restarting therapy).

Jones JR, Pawlyn C, Davies FE, Morgan GJ. The safety of pomalidomide for the treatment of multiple myeloma. Expert Opin Drug Saf. 2016;15:535–47. PubMed PMID: 26913560.

(Review of the chemical structure, mechanism of action and safety of pomalidomide, mentions that monitoring of liver tests is recommended and that individual case reports of liver injury have been reported).

Tsukune Y, Sasaki M, Odajima T, Sunami K, Takei T, Moriuchi Y, Iino M, et al. Incidence and risk factors of hepatitis B virus reactivation in patients with multiple myeloma in an era with novel agents: a nationwide retrospective study in Japan. Blood Cancer J. 2017;7:631. PubMed PMID: 29167420.

(Japanese nationwide analysis of 5078 patients with multiple myeloma identified 760 with resolved hepatitis B [anti-HBc without HBsAg in serum] of whom 7.6% developed reactivation [7.9% at 2 and 14.1% at 5 years], multivariate analysis demonstrating higher rates in those undergoing autologous hematopoietic stem cell transplant [21%:odds ratio=11.6] and lower rates in those receiving lenalidomide [5.2%:odds ratio=0.5], but not thalidomide, bortezomib or dexamethasone).

Reed-Guy L, Hoteit MA, Garfall AL. Acute liver failure associated with pomalidomide therapy for multiple myeloma. Clin Lymphoma Myeloma Leuk. 2018;18:e337–e338. PubMed PMID: 29907543.

(56 year old man with refractory, relapsed multiple myeloma developed fever and jaundice 4 days after starting pomalidomide [bilirubin 4.6 mg/dL, ALT 907 U/L, AST 1518 U/L, LDH 1974 U/L, Alk P 92 U/L, INR 2.8, creatinine 1.9 mg/dL], with rapid improvement on stopping therapy, normal ALT and INR 2 weeks later).

Garderet L, Kuhnowski F, Berge B, Roussel M, Escoffre-Barbe M, Lafon I, Facon T, et al. Pomalidomide, cyclophosphamide, and dexamethasone for relapsed multiple myeloma. Blood. 2018;132:2555–2563. PubMed PMID: 30282798.

(Among 97 patients with relapsed multiple myeloma treated with pomalidomide, cyclophosphamide and dexamethasone, the objective response rate was 85% and adverse event rate [grade 3 or 4] was 70%, which were largely hematologic [62%] and infections [6%]; no hepatic events were listed).

Parisi MS, Leotta S, Romano A, Del Fabro V, Martino EA, Calafiore V, Giubbolini R, et al. Clinical benefit of long-term disease control with pomalidomide and dexamethasone in relapsed/refractory multiple myeloma patients. J Clin Med. 2019;8:1695. PubMed PMID: 31623097.

(Among 76 patients with relapsed or refractory multiple myeloma treated with pomalidomide and dexamethasone in a Italian national program, severe [grade 3] adverse events included hematologic [51%] and non-hematologic effects [32%], which were mostly infections and none of which were hepatic).

Kikuchi T, Kusumoto S, Tanaka Y, Oshima Y, Fujinami H, Suzuki T, Totani H, et al. Hepatitis B virus reactivation in a myeloma patient with resolved infection who received daratumumab-containing salvage chemotherapy. J Clin Exp Hematop. 2020;60:51–54. PubMed PMID: 32404569.

(72 year old women with multiple myeloma who was negative for HBsAg but positive for anti-HBc without anti-HBs was monitored and had no evidence for reactivation during multiple courses of bortezomib, melphalan, dexamethasone, lenalidomide and pomalidomide over a 3 year period, but then developed HBV DNA [2.2 to 2.6 log_{10} per mL] and HBsAg after 3rd course of daratumumab with bortezomib and dexamethasone with rapid response upon addition of entecavir).

Curtis LM, Ostojic A, Venzon DJ, Holtzman NG, Pirsl F, Kuzmina ZJ, Baird K, et al. A randomized phase 2 trial of pomalidomide in subjects failing prior therapy for chronic graft-versus-host disease. Blood. 2021;137:896–907. PubMed PMID: 32976576.

(Among 34 patients with moderate to severe chronic graft-vs-host disease treated with pomalidomide [0.5 or 2 mg daily], the objective response rate was 67% but all responses were partial, the most common adverse events were lymphopenia [68%], infection [47%] and fatigue [41%], and while ALT elevations above 5 times ULN arose in 6% there were cases of clinically apparent liver injury).

Terpos E, Repousis P, Lalayanni C, Hatjiharissi E, Assimakopoulou T, Vassilopoulos G, Pouli A, et al. Pomalidomide plus low-dose dexamethasone in relapsed/refractory multiple myeloma patients: results of the real-world "POWERFUL" study. J Clin Med. 2021;10:1509. PubMed PMID: 33916376.

(Among 99 patients with relapsed or refractory multiple myeloma treated with pomalidomide and dexamethasone in a Greek National program, the response rate was 32%, and 80% of patients had at least one adverse event including 8% with hematologic and 5% with non-hematologic grade 3 events, none of which were hepatic).

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(Among 144 patients with relapsed or refractory multiple myeloma treated with pomalidomide and dexamethasone in a German observational study, the overall response rate was 32% and treated related adverse events arose in 63%, which were severe [grade 3-4] in 36%, none of which were liver related).

Ramaswami R, Polizzotto MN, Lurain K, Wyvill KM, Widell A, George J, Goncalves P, et al. Safety, activity, and long-term outcomes of pomalidomide in the treatment of Kaposi sarcoma among individuals with or without HIV Infection. Clin Cancer Res. 2022;28:840–850. PubMed PMID: 34862247.

(Among 28 patients with Kaposi sarcoma [18: 65% with HIV infection] treated with pomalidomide [5 mg daily for 21 of each 28-day cycle], the objective response rate was 71% and adverse events were common including ALT elevations in 25%, all of which were transient, asymptomatic and less than 3 times ULN).