Prednisone and Azathioprine Compared With Prednisone and Placebo for Treatment of Chronic Graft-*v*-Host Disease: Prognostic Influence of Prolonged Thrombocytopenia After Allogeneic Marrow Transplantation

By K.M. Sullivan, R.P. Witherspoon, R. Storb, P. Weiden, N. Flournoy, S. Dahlberg, H.J. Deeg, J.E. Sanders, K.C. Doney, F.R. Appelbaum, R. McGuffin, G.B. McDonald, J. Meyers, M.M. Schubert, J. Gauvreau, H.M. Shulman, G.E. Sale, C. Anasetti, T.P. Loughran, S. Strom, J. Nims, and E.D. Thomas

We conducted a randomized, double-blind comparison of prednisone and placebo (group I) *v* prednisone and azathioprine (1.5 mg/kg/day) (group II) as early treatment of extensive chronic graft-*v*-host disease (GVHD). Patients with platelet counts <100,000/μL were placed into therapy with prednisone alone (group III). All three groups received identical doses of prednisone (1 mg/kg every other day) and one double-strength trimethoprim-sulfamethoxazole (TMP-SMX) tablet twice daily. Between January 1980 and December 1983, 179 previously untreated patients were enrolled and 164 were evaluable. Patients randomized to group I (n = 63) and group II (n = 63) were well matched for prognostic factors; those placed into group III (n = 38) had more frequent acute GVHD and progressive onset of chronic GVHD. Median duration of therapy was 2 years. Complications included diabetes (5%), aseptic necrosis (5%) and infection. For groups I, II, and III, the respective incidence of infection was disseminated varicella, 11%, 24%, 34%; bacteremia, 6%, 11%, 34%; and interstitial pneumonia, 5%, 14%, 18%. Recurrent malignancy was the most frequent cause of death and did not differ significantly across the groups. Nonrelapse mortality, however, did differ: 21% in group I, 40% in group II, and 58% in group III (I *v* II, *P* = .003; I *v* III, *P* = .001). Forty patients in group I, 30 in group II, and 10 in group III survive with a minimum follow-up of 3.8 years. Karnofsky performance scores for 68 survivors are 90% to 100%, scores for seven survivors are 70% to 89% and scores for five survivors are <70%. Actuarial survival at 5 years after transplant is 61% in group I, 47% in group II, and 26% in group III (I *v* II, *P* = .03; I *v* III, *P* = .0001). Treatment with prednisone alone results in fewer infections and better survival than prednisone and azathioprine in standard-risk chronic GVHD. Treatment with prednisone alone is less effective in high-risk patients with thrombocytopenia, and other strategies are required.
© 1988 by Grune & Stratton, Inc.

CHRONIC graft-*v*-host disease (GVHD) is a major late complication in 25% to 45% of survivors of allogeneic marrow transplantation.[1-3] Less than 20% of patients with untreated extensive chronic GVHD survive with Karnofsky performance scores ≥70%.[2] Therapy with antithymocyte globulin or corticosteroids given late in the course of disease results in little benefit.[2] In a pilot study of combined immunosuppression with cytotoxic agents and corticosteroids, 16 of 21 patients survive free of disability.[2] However, comparison of therapy with azathioprine and prednisone to our previous experience with prednisone alone was complicated by the fact that patients given the combination were treated in more recent times when earlier diagnosis and therapy, better supportive care and closer follow-up were used.

Because the benefits and toxicities of long-term cytotoxic therapy after marrow grafting are unclear, we studied in a randomized, double-blind trial the use of prednisone and placebo compared with prednisone and azathioprine in early treatment of chronic GVHD. Patients with poor marrow function as a contraindication to azathioprine (platelet counts <100,000/μL) were placed into treatment with prednisone alone. We report the results of this controlled clinical trial, which has a minimum follow-up of 3.8 years after transplant.

MATERIALS AND METHODS

From January 1980 to December 1983, 179 patients with extensive (multiorgan) chronic GVHD entered the study. Seventy enrolled patients were randomized to receive prednisone and placebo (group I), and 71 were randomized to receive prednisone and azathioprine (group II). An additional 38 patients with thrombocytopenia (group III) were placed into treatment with prednisone alone. When an interim analysis showed an increased mortality,[4] group III was closed and treatment was modified to include alternating cyclosporine and prednisone. Results of that subsequent study were presented in another report.[5]

Fifteen (11%) of 141 enrolled patients randomized to groups I and II had violations of the double-blind treatment protocol and were not evaluable for response. Five patients refused treatment after enrollment because they considered that therapy was not required. Five refused the study drug and two took open-label azathioprine because they or their physicians wished to choose the specific drug regimen. The remaining three patients discontinued treatment before completing the 9-month schedule. The results in these 15 inevaluable patients were as follows. In group I, three refused therapy (two died and one survived with 40% performance); one stopped treatment after 3 months and died; one refused study drug, took prednisone and azathioprine, and died; and two refused study drug and took

From the Fred Hutchinson Cancer Research Center and the University of Washington School of Medicine, Seattle.

Submitted August 12, 1987; accepted March 29, 1988.

Supported by US Public Health Service Grants No. CA 18221, CA 18029, CA 09515, CA 15704 from the National Cancer Institute, and HL 36444 from the National Institute of Heart, Lung and Blood, Department of Health and Human Services.

Presented in part at the 29th Annual Meeting of the American Society of Hematology, Washington, DC, December 5-8, 1987.

Dr Thomas is a recipient of Research Career Award AI 02425 from the National Institute of Allergy and Infectious Diseases, DHHS. Dr. Loughran is a Fellow of the Leukemia Society of America.

Address reprint requests to Keith M. Sullivan, MD, Fred Hutchinson Cancer Research Center, Department of Medicine, Division of Oncology, 1124 Columbia St, Seattle, WA 98104.

The publication costs of this article were defrayed in part by page charge payment. This article must therefore be hereby marked "advertisement" *in accordance with 18 U.S.C. section 1734 solely to indicate this fact.*

© 1988 by Grune & Stratton, Inc.

0006-4971/88/7202-0019$3.00/0

DOCKET ALARM

Pharmacyclics Exhibit 2057 - Page 1 of 9
Sandoz v. Pharmacyclics - IPR2019-00865

Find authenticated court documents without watermarks at docketalarm.com.

prednisone (both survive with 100% performance). In group II, two refused therapy (both died); three refused study drug (one died, one survived with 50% performance, and one survived with 100% performance); one complied poorly with treatment and died; one refused study drug, took prednisone and azathioprine, and died; and one stopped treatment after 6 months and survived with 100% performance.

Demographic data of 164 evaluable patients are listed in Table 1. Patients with aplastic anemia were prepared for transplant with cyclophosphamide, 50 mg/kg on each of four successive days.[6] Patients with hematologic malignancies received high-dose cyclophosphamide or other chemotherapy regimens followed by total body irradiation (TBI) given as a single 10-Gy dose or as a fractionated 12- to 17.5-Gy dose.[7,8] All but 14 patients received marrow from HLA-identical siblings; those 14 received marrow from HLA-nonidentical donors.[9] Three HLA-identical recipients

Table 1. Patient Characteristics at Study Entry

Characteristic	Randomized		Placed
	Prednisone + Placebo (Group I)	Prednisone + Azathioprine (Group II)	Prednisone Alone (Group III)
No. of evaluable patients	63	63	38
Diagnosis			
Aplastic anemia	9	7	2
Refractory ANL/ALL	2/0	4/0	0/0
Relapse ANL/ALL	6/6	8/6	1/3
2nd+ Remission ANL/ALL	1/10	1/3	2/8
1st Remission ANL/ALL	13/3	12/3	11/1
Accelerated or blast crisis CML	4	8	4
Chronic phase CML	7	7	4
Lymphoma/other	2/0	2/2	2/0
No. (%) of patients			
<10 yr	8 (13)	5 (8)	6 (16)
10-30 yr	42 (66)	44 (70)	22 (58)
>30 yr	13 (21)	14 (22)	10 (26)
Median (range) age in years	23 (2-43)	24 (1-48)	23 (3-47)
Sex (M/F)	44/19	47/16	28/10
HLA-nonidentical donor (%)	4 (6)	4 (6)	6 (16)
Bone marrow T-cell depletion	1	1	1
Acute GVHD prophylaxis			
None	0	0	0
Short MTX (11 d)	5	6	1
Standard MTX (102 d)	46	49	35
Cyclosporine (180 d)	9	5	2
MTX/cyclosporine (11/180 d)	3	3	0
Grade of Acute GVHD			
0	21	24	8
I	13	12	6
II	19	11	9
III	10	16	14
IV	0	0	1
Total grade II-IV (%)	29 (46)	27 (43)	24 (63)
Type of onset of chronic GVHD (%)			
De novo	21 (33)	24 (38)	8 (21)
Quiescent	31 (49)	27 (43)	17 (45)
Progressive	11 (17)	12 (19)	13 (34)
Presentation of chronic GVHD (%)			
Subclinical always	6 (10)	8 (13)	5 (13)
Subclinical → clinical	18 (28)	17 (27)	9 (24)
Clinical always	39 (62)	38 (60)	24 (63)
No. (%) Entering treatment			
≤4 mo after transplant	35 (56)	34 (54)	33 (87)
5-12 mo after transplant	21 (33)	26 (41)	5 (13)
>12 mo after transplant	7 (11)	3 (5)	0
Median (range) values at entry			
Time to treatment (months after transplant)	3 (2-38)	4 (2-33)	3 (3-8)
Karnofsky score (%)	70 (60-95)	70 (30-100)	70 (30-90)
Serum bilirubin (mg/dl)	0.9 (0.2-14.0)	0.7 (0.2-39.0)	1.0 (0.1-14.0)
WBC count ($\times 10^3/\mu L$)	5.4 (1.6-19.0)	5.4 (2.2-20.0)	4.3 (1.5-14.8)
Platelet count ($\times 10^3/\mu L$)	170 (100-442)	168 (100-600)	39 (6-80)

Abbreviations: ALL, acute lymphoblastic leukemia; ANL, acute nonlymphoblastic leukemia; CML, chronic myelogenous leukemia; GVHD, graft-*v*-host disease; MTX, methotrexate.

DOCKET ALARM
Pharmacyclics Exhibit 2057 - Page 2 of 9
Sandoz v. Pharmacyclics - IPR2019-00865
Find authenticated court documents without watermarks at docketalarm.com.

were given marrow purged of T lymphocytes.[10] All others received unmodified allogeneic marrow. The prophylaxis, grading, and treatment of acute GVHD were reported previously.[11-15]

Chronic GVHD had a progressive onset if it followed as a direct extension of acute GVHD. Quiescent chronic GVHD developed after resolution of acute GVHD, whereas de novo chronic GVHD was not preceded by acute GVHD. Diagnosis was established upon review of clinical, laboratory, and histologic data by previously published criteria.[2,16] Subclinical chronic GVHD was defined as histologic evidence of chronic GVHD on both the blind skin and oral biopsies without signs or symptoms of clinical disease. Clinical chronic GVHD was defined as both histologic and clinical evidence of chronic GVHD. At study entry, all patients were in hematologic remission with donor marrow engraftment and had not received prior treatment for chronic GVHD. Previous GVHD prophylaxis was discontinued upon study entry.

Protocols and consent forms were approved by the Institutional Review Board of the Fred Hutchinson Cancer Research Center. All three groups received prednisone given in oral divided doses for weeks 1 and 2 and thereafter as a single oral morning dose (Table 2). Patients in groups I and II received study drug in addition to prednisone. Study drug was assigned by random permutations of a set of numbers known only to the protocol registrar and was supplied as unmarked 50-mg scored tablets of either placebo or azathioprine. Study drug was given as a single evening dose of 1.5 mg/kg/day.

Patients in all three treatment groups received prophylactic TMP-SMX. Adults received one double-strength (160 mg TMP) tablet twice daily, and children received 75 mg/m^2 TMP twice daily. Patients with life-threatening TMP-SMX allergies received prophylactic penicillin or cephalexin. Patients with less severe allergic histories were rechallenged with TMP-SMX. Patients received supportive care with artificial tear replacements, sun-blocking creams, and oral caloric and protein supplements as required.

After 9 months of treatment, patients were reevaluated in Seattle with physical examination, assessment of Karnofsky performance score, laboratory studies (blood urea nitrogen, serum creatinine, complete blood count, and liver function tests), pulmonary function tests, Schirmer's test and biomicroscopy, nutritional status, and routine skin and oral mucosa biopsies and other biopsies as indicated.[17,18] The drug code was not broken and response to treatment was determined in a blinded manner. The following criteria were used to judge treatment response. Progressive disease after 2 months of treatment or stable disease with persisting Karnofsky scores <50% after 9 months of treatment was considered no response. The drug code was broken at study failure. Clinically inactive chronic GVHD, but biopsies showing continued GVHD activity with no new organ involvement after 9 months of therapy was considered partial response. Clinically inactive disease and biopsies showing no GVHD activity after 9 months of therapy was considered complete response. When treatment was stopped after a complete response but clinical and histologic disease activity returned, the patient was considered to have a flare of chronic GVHD. Therapy was reinstituted for another 9 months. For patients with a complete response, therapy was discontinued. For patients with a partial response, treatment continued. If chronic GVHD symptoms were clinically active and disabling after 18 months of treatment, patients were declared a failure.

Results were analyzed as of June 1, 1987. Survival rates were estimated by the Kaplan-Meier method, and comparison statistics (two-sided significance levels) were calculated using the log-rank and stratified log-rank tests.[19,20]

Table 2. Alternate-Day Prednisone Regimen

	Prednisone (mg/kg/orally)	
Week of Therapy	Day A	Day B
1	1.0	1.0
2	1.0	1.0
3	2.0	0.5
4	2.0	0.25
5	2.0	0.12
6	2.0	0
7	1.5	0
8	1.25	0
9-36	1.0	0

RESULTS

Entry data. As shown in Table 1, patients randomized to groups I and II were well matched for treatment and prognostic factors. Twenty-four (38%) patients in group I, 25 (40%) in group II, and 14 (37%) in group III started treatment while chronic GVHD was still subclinical. Forty-four (70%) of these 63 patients with subclinical disease at diagnosis developed clinical chronic GVHD during treatment. Only in 19 (12%) of the 164 evaluable patients did chronic GVHD remain subclinical throughout therapy.

Patients in group III did not appear to differ from randomized patients in diagnosis, age, acute GVHD prophylaxis, pretreatment Karnofsky scores or bilirubin values, or time to treatment. By definition, all had platelet counts <100,000/μL. The leukocyte counts were slightly lower in group III patients, but only two patients had leukocytes <2,000/μL at entry. Median pretreatment bone marrow cellularity was 80% of normal in group I, 80% of normal in group II, and 50% of normal in group III.

Response. Nine months after starting therapy, 47 (29%) of 164 evaluable patients had died or relapsed, 26 (16%) had failed therapy, and 41 (25%) had a partial response and 50 (30%) had a complete response to treatment (Table 3). Complete responses occurred in 21 (33%) patients of group I, 23 (37%) of group II, and six (16%) of group III.

Long-term follow-up. Among 117 patients surviving in hematologic remission who completed 9 months of therapy (Table 3), 50 (93%) of 54 patients in group I, 40 (89%) of 45 patients in group II, and 15 (83%) of 18 patients in group III returned one or more times to Seattle for reevaluation.

Toxicity and infection. Thirty (18%) of the 164 evaluable patients developed one or more of the toxicities listed in Table 3. Twenty-nine (46%) patients in group I, 39 (62%) in group II, and 28 (74%) in group III developed one or more infections listed in Table 3. Disseminated varicella zoster, bacteremia, and interstitial pneumonia were more frequent in patients randomized to receive azathioprine as compared with placebo recipients. Patients in group III had more frequent infections than did patients in group I who received identical treatment.

Among 28 episodes of bacteremia, eight were owing to pneumococcus (five occurring when patients were off TMP-SMX), six *Staphylococcus,* six *Pseudomonas,* five *Hemophilus influenzae,* and three other gram-negative organisms. Twenty episodes of interstitial pneumonia (six *Pneumocystis pneumoniae,* five varicella, four idiopathic, three cytomegalovirus (CMV), one *Legionella,* and one herpes simplex)

DOCKET ALARM
Pharmacyclics Exhibit 2057 - Page 3 of 9
Sandoz v. Pharmacyclics - IPR2019-00865
Find authenticated court documents without watermarks at docketalarm.com.

Table 3. Results of Treatment

Result	Randomized		Placed
	Prednisone + Placebo (Group I)	Prednisone + Azathioprine (Group II)	Prednisone Alone (Group III)
No. of evaluable patients	63	63	38
Response (%) after 9-mo therapy			
Complete response	21 (33)	23 (37)	6 (16)
Partial response	18 (29)	17 (27)	6 (16)
Failed treatment	15 (24)	5 (8)	6 (16)
Died or Relapsed before 9 mo	9 (14)	18 (29)	20 (52)
Median (range) Karnofsky score after 9-mo therapy (%)			
Complete responders	100 (90-100)	100 (80-100)	100 (90-100)
Partial responders	95 (80-100)	90 (80-100)	90 (80-100)
Failed treatment	70 (30-95)	30 (30-90)	70 (50-90)
Toxicity of therapy			
Diabetes mellitus	3	5	1
Aseptic necrosis	4	3	1
Neutrophils $<1,000/\mu L$	0	4	2
Platelets $<100,000/\mu L$	1	3	—
Gastrointestinal hemorrhage	1	2	2
Severe osteoporosis	1	0	1
Psychosis	1	0	0
Episodes of infection (no. of patients, percentage of patients)			
Varicella zoster (total)	18 (18, 29%)	25 (25, 40%)	17 (15, 39%)
Localized	11 (11, 17%)	10 (10, 16%)	2 (2, 5%)
Disseminated	7 (7, 11%)	15 (15, 24%)	15 (13, 34%)
Bacteremia	4 (4, 6%)	7 (7, 11%)	17 (13, 34%)
Interstitial pneumonia	3 (3, 5%)	9 (9, 14%)	8 (7, 18%)
Noninterstitial pneumonia	13 (10, 16%)	14 (10, 16%)	17 (13, 34%)

were observed. All six episodes of *Pneumocystis pneumoniae* developed in 31 patients either not given or discontinuing TMP-SMX. Forty-four episodes of noninterstitial pneumonia developed, 21 owing to unknown organisms and the remainder owing to *Pneumococcus* (11), *Hemophilus influenzae* (four), fungus (four), gram-negative organisms (two) and staphylococcus (two).

Drug dosage. Prednisone was given in the first 9 months in full dose schedule to 141 (86%) patients; the remaining patients had some dose modifications owing to the toxicities listed in Table 3. Permanent reduction in prednisone dose was observed in eight (5%) patients: three to 75% to 99%, three to 50% to 74%, and two to 25% to 40% protocol dose. Azathioprine was given in reduced dose in four (6%) patients: two to 75% to 99% and two to 50% to 74% protocol dose. Prophylactic TMP-SMX was not given or was discontinued owing to side effects in nine (14%) patients in group I, nine (14%) in group II, and 13 (34%) in group III. Twelve of these 31 patients received no additional antibiotics. The remaining 19 received cephalexin (nine), penicillin (eight), or ampicillin (two).

Clinical manifestations. Sites of disease noted in 145 patients with clinical chronic GVHD were dermal (79%), hepatic (73%), oral (72%), ophthalmic (47%), intestinal (16%), myofascial (11%), pulmonary (11%), esophageal (6%), and serosal (2%). Intestinal chronic GVHD was more frequent in patients in group III. Laboratory abnormalities included rheumatoid factor reactivity (16%), hypogammaglobulinemia (IgG < 650 mg/dL, 15%) and autoantibody production (8%). Scleroderma with joint contractures developed in 11 (8%) of 145 evaluable patients with clinical chronic GVHD.

Mortality. Twenty-three (37%) patients in group I, 33 (52%) in group II, and 28 (74%) in group III died (Table 4). Recurrent malignancy was the most common cause of death. Kaplan-Meier estimates of recurrent malignancy were 26% in group I, 33% in group II, and 39% in group III (I *v* II, $P = .95$; I *v* III, $P = .23$). Infection was the most common cause of nonrelapse mortality. The remaining deaths were owing to progressive GVHD without infection, hemorrhage, or organ failure. One patient with a long pretransplant history of paranoia refused psychiatric therapy and committed suicide.

Figure 1 shows the probability of death from nonrelapse causes. By actuarial estimate, 21% of patients in group I, 40% in group II, and 58% in group III died of nonmalignant causes ($P = .0001$). Among randomized patients, nonrelapse mortality was significantly increased in azathioprine recipients ($P = .003$). When group I was compared to group III, the increase in nonrelapse mortality in patients with thrombocytopenia was significant ($P = .0001$).

Prognostic factors. Mortality did not appear related to gender, acute GVHD prophylaxis, or time to study entry. Table 5 lists factors in relation to mortality from all causes. Age >20 years ($P = .02$), prior grade II through IV acute GVHD ($P = .03$), the progressive onset of chronic GVHD ($P = .0001$), and failure to respond to 9 months of treatment ($P = .04$) were associated with increased mortality in log-rank analyses stratified by treatment group.

Actuarial mortality in 19 patients in whom chronic

DOCKET ALARM
Pharmacyclics Exhibit 2057 - Page 4 of 9
Sandoz v. Pharmacyclics - IPR2019-00865
Find authenticated court documents without watermarks at docketalarm.com.

Table 4. Causes of Death

Cause	Randomized: Prednisone + Placebo (n = 63)	Randomized: Prednisone + Azathioprine (n = 63)	Placed: Prednisone Alone (n = 38)
Bacterial infection	2	10	6
Interstitial pneumonia			
Varicella zoster	1	1	2
Cytomegalovirus	0	0	2
Idiopathic	0	2	0
Pneumocystis	0	1	0
Other Infection	1	1	0
Fungal infection	1	3	3
Progressive GVHD without infection	1	1	1
Respiratory failure without IP	1	1	1
Heart failure	0	1	1
Varicella zoster without IP	1	1	0
Hemorrhage	0	1	1
Myasthenia gravis	0	0	1
Suicide	1	0	0
Recurrent malignancy	14	10	10
Total	23	33	28

Abbreviations: GVHD, graft-versus-host disease; IP, interstitial (nonbacterial, nonfungal) pneumonia.

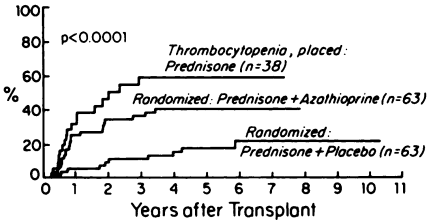

Fig 1. Kaplan-Meier product limit estimates of the probability of death from nonrelapse (ie, transplant-related) causes.

GVHD remained subclinical throughout therapy was 58% as compared with 50% mortality in 46 patients with subclinical → clinical chronic GVHD and 52% mortality in 99 patients with clinical chronic GVHD at diagnosis. Patients with sustained subclinical chronic GVHD had higher mortality owing to an increased rate of relapse of leukemia. Figure 2 shows the probability of relapse in 146 patients with hematologic malignancies in relation to the course of chronic GVHD. Three-way statistical analysis showed that relapse of malignancy was significantly increased in patients in whom chronic GVHD remained subclinical throughout observation ($P = .0003$).

Table 5. Mortality Risk Factors

Factor	No. of Dead/No. of Evaluable Patients: Group I (n = 63)	Group II (n = 63)	Group III (n = 38)	Total (%) (n = 164)
Patient age				
≤20 yr	8/31	6/17	11/17	25/65 (38)
>20 yr	15/32	27/46	17/21	59/99 (60)
Grade acute GVHD				
0	6/21	10/24	4/8	20/53 (38)
I	5/13	7/12	4/6	16/31 (52)
II	6/19	6/11	8/9	20/39 (51)
III	6/10	10/16	11/14	27/40 (68)
IV	0/0	0/0	1/1	1/1 (100)
Type of chronic GVHD onset				
De novo	6/21	10/24	4/8	20/53 (38)
Quiescent	12/31	14/27	12/17	38/75 (51)
Progressive	5/11	9/12	12/13	26/36 (72)
Presentation of chronic GVHD				
Subclinical always	3/6	4/8	4/5	11/19 (58)
Subclinical → clinical	7/18	6/17	7/9	20/44 (45)
Clinical always	13/39	23/38	17/24	53/101 (52)
Response after 9-mo therapy				
Complete response	2/21	7/23	1/6	10/50 (20)
Partial response	5/18	4/17	4/6	13/41 (31)
Failed treatment	7/15	4/5	3/6	14/26 (54)
Died or relapsed before 9 mo	9	18	20	47

Pharmacyclics Exhibit 2057 - Page 5 of 9
Sandoz v. Pharmacyclics - IPR2019-00865
DOCKET ALARM
Find authenticated court documents without watermarks at docketalarm.com.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.