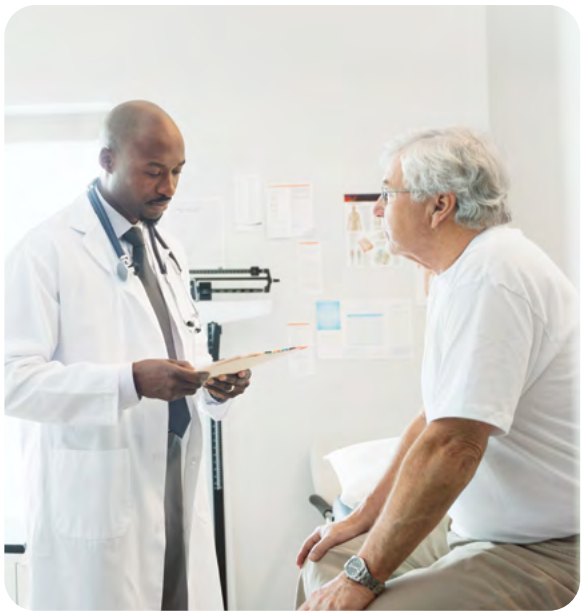
HALAVEN®

A treatment option for patients with advanced **liposarcoma**



Indication

Liposarcoma

HALAVEN (eribulin mesylate) Injection is indicated for the treatment of patients with unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen.

Selected Safety Information

Warnings and Precautions

Neutropenia: Severe neutropenia (ANC <500/mm^3) lasting >1 week occurred in 12% of patients with liposarcoma or leiomyosarcoma. Febrile neutropenia occurred in 0.9% of patients and fatal neutropenic sepsis occurred in 0.9% of patients. Monitor complete blood cell counts prior to each dose, and increase the frequency of monitoring in patients who develop Grade 3 or 4 cytopenias. Delay administration and reduce subsequent doses in patients who experience febrile neutropenia or Grade 4 neutropenia lasting >7 days.

Please see all Selected Safety Information throughout and full Prescribing Information.

Halaven®
(eribulin mesylate) Injection | 0.5 mg/mL

HALAVEN® was studied in a Phase III trial in patients with intermediate-to-high tumor grades, regardless of liposarcoma subtype[1-3]*

Liposarcoma subtype	% of patients with liposarcoma
Dedifferentiated	45%
Myxoid/round cell	37%
Pleomorphic	18%

Performance status	% of patients with liposarcoma
ECOG PS 0	41%
ECOG PS 1	53%

Tumor grade	% of patients with liposarcoma
High	54%
Intermediate	45%

ECOG PS=Eastern Cooperative Oncology Group performance status.

*A total of 446 patients with locally advanced or metastatic liposarcoma or leiomyosarcoma were included in the Phase III study. 32% and 68% of patients included had liposarcoma and leiomyosarcoma, respectively.[1,3]

Both dedifferentiated and pleomorphic subtypes have historically shown low responsiveness to treatment regimens[4]

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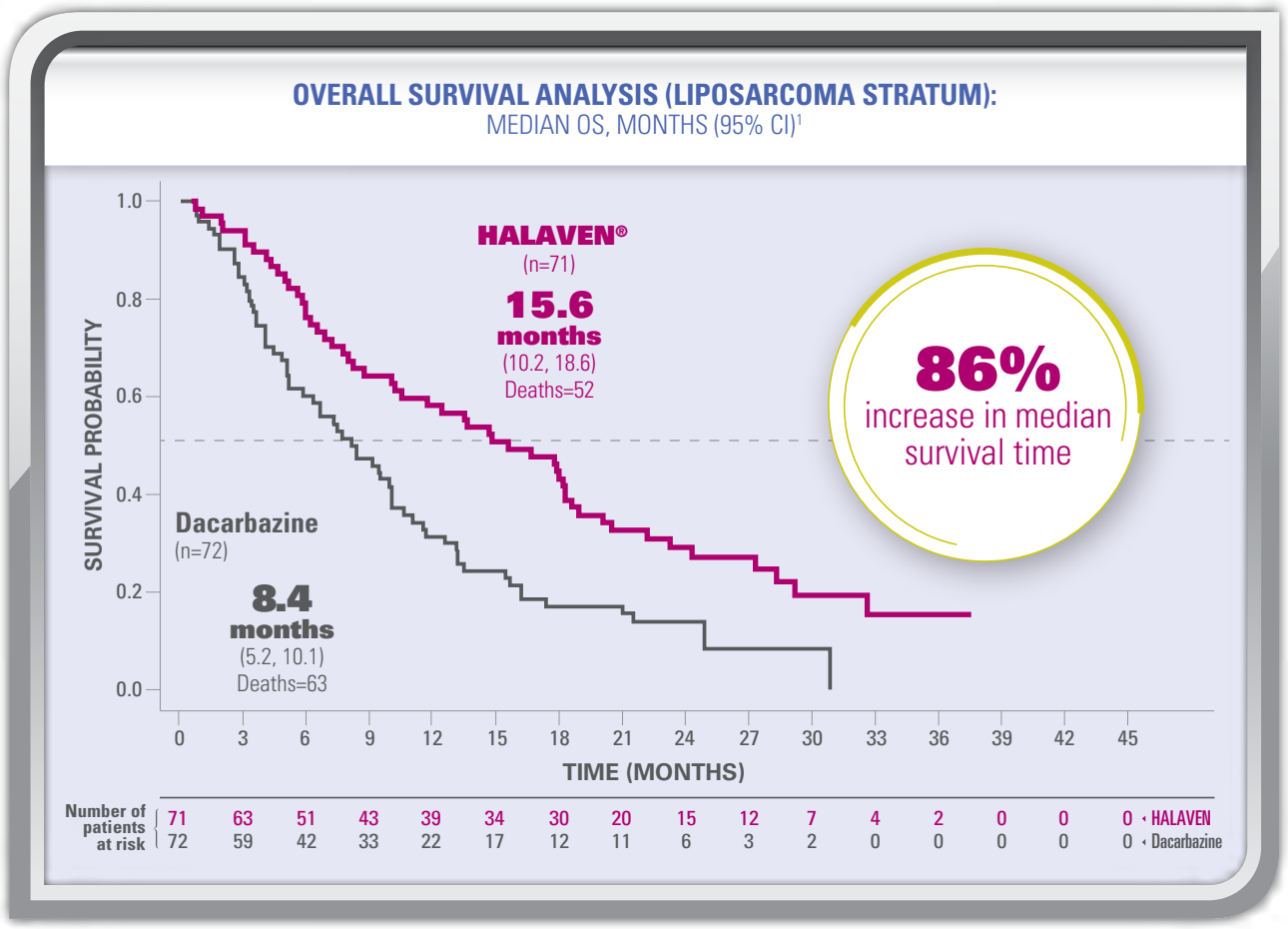
The first and only single agent to show a significant survival advantage in a Phase III study of patients with advanced liposarcoma[3]



The efficacy and safety of HALAVEN were evaluated in an open-label, randomized (1:1), multicenter, active-controlled trial. Eligible patients were required to have unresectable, locally advanced or metastatic liposarcoma or leiomyosarcoma, at least 2 prior systemic chemotherapies (1 of which must have included an anthracycline), and disease progression within 6 months of the most recent chemotherapy regimen. Patients were randomized to HALAVEN 1.4 mg/m^2 administered intravenously on Days 1 and 8 of a 21-day cycle or to dacarbazine at a dose of 850 mg/m^2, 1,000 mg/m^2, or 1,200 mg/m^2 administered intravenously every 21 days (dacarbazine dose was selected by the investigator prior to randomization). Treatment continued until disease progression or unacceptable toxicity. Randomization was stratified by histology (liposarcoma or leiomyosarcoma), number of prior therapies (2 vs >2), and geographic region. The most common (>40%) prior systemic chemotherapies were doxorubicin (90%), ifosfamide (62%), gemcitabine (59%), trabectedin (50%), and docetaxel (48%).[1]

OS=overall survival; CI=confidence interval.

Selected Safety Information

Peripheral Neuropathy: Grade 3 peripheral neuropathy occurred in 3.1% of patients with liposarcoma and leiomyosarcoma receiving HALAVEN and neuropathy lasting more than 60 days occurred in 58% (38/65) of patients who had neuropathy at the last treatment visit. Patients should be monitored for signs of peripheral motor and sensory neuropathy. Withhold HALAVEN in patients who experience Grade 3 or 4 peripheral neuropathy until resolution to Grade 2 or less.

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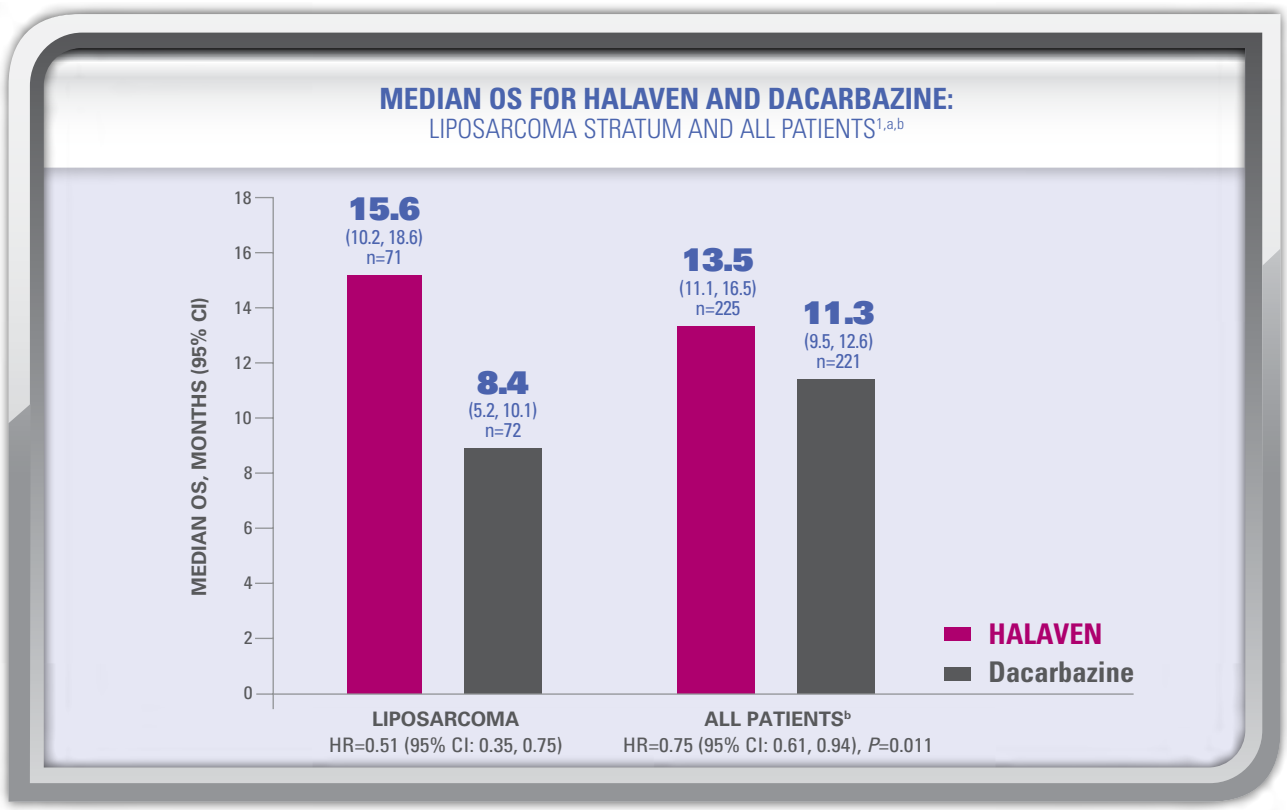
Treatment effects of HALAVEN® were demonstrated in patients with advanced liposarcoma based on the preplanned, exploratory subgroup analyses of OS and PFS[1]



PFS=progression-free survival; HR=hazard ratio.
[a]Efficacy data from 1 study site enrolling 6 patients were excluded.
[b]All patients=liposarcoma and leiomyosarcoma.

- There was no evidence of efficacy of HALAVEN in patients with advanced or metastatic leiomyosarcoma in this trial[1]

Secondary endpoint: PFS[1]

- Median PFS in the liposarcoma stratum was 2.9 months (95% CI: 2.6, 4.8) for patients receiving HALAVEN vs 1.7 months (95% CI: 1.4, 2.6) for patients receiving dacarbazine, HR=0.52 (95% CI: 0.35, 0.78)
- Median PFS in all patients was 2.6 months (95% CI: 2.0, 2.8) for patients receiving HALAVEN vs 2.6 months (95% CI: 1.7, 2.7) for patients receiving dacarbazine, HR=0.86 (95% CI: 0.69, 1.06)

Selected Safety Information

Embryo-Fetal Toxicity: HALAVEN can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with HALAVEN and for at least 2 weeks following the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with HALAVEN and for 3.5 months following the final dose.

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Eisai is committed to *human health care (hhc)*

Eisai's commitment to innovative solutions in disease prevention and care for the health and well-being of people worldwide is embodied in our *hhc* mission. Human health care means we give first thoughts to patients and their families by helping to ensure access to necessary medicines.

For more information about HALAVEN®, please visit
www.halaven.com

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HALAVEN® offers a significant overall survival benefit for your patients with advanced liposarcoma[1]

HALAVEN improved median OS in advanced liposarcoma vs dacarbazine (15.6 months vs 8.4 months) in a Phase III study.[1,3]

To learn more about HALAVEN, please visit
www.halaven.com/hcp/advanced-liposarcoma

Selected Safety Information

QT Prolongation: Monitor for prolonged QT intervals in patients with congestive heart failure, bradyarrhythmias, drugs known to prolong the QT interval, and electrolyte abnormalities. Correct hypokalemia or hypomagnesemia prior to initiating HALAVEN and monitor these electrolytes periodically during therapy. Avoid in patients with congenital long QT syndrome.

Adverse Reactions

In patients with liposarcoma and leiomyosarcoma receiving HALAVEN, the most common adverse reactions (≥25%) reported in patients receiving HALAVEN were fatigue (62%), nausea (41%), alopecia (35%), constipation (32%), peripheral neuropathy (29%), abdominal pain (29%), and pyrexia (28%). The most common (≥5%) Grade 3-4 laboratory abnormalities reported in patients receiving HALAVEN were neutropenia (32%), hypokalemia (5.4%), and hypocalcemia (5%). Neutropenia (4.9%) and pyrexia (4.5%) were the most common serious adverse reactions. The most common adverse reactions resulting in discontinuation were fatigue and thrombocytopenia (0.9% each).

Use in Specific Populations

Lactation: Because of the potential for serious adverse reactions in breastfed infants from eribulin mesylate, advise women not to breastfeed during treatment with HALAVEN and for 2 weeks after the final dose.

Hepatic and Renal Impairment: A reduction in starting dose is recommended for patients with mild or moderate hepatic impairment and/or moderate or severe renal impairment.

References: 1. HALAVEN [package insert]. Woodcliff Lake, NJ: Eisai Inc. **2.** Data on file, Eisai Inc. **3.** Schöffski P, Chawla S, Maki RG, et al. Eribulin versus dacarbazine in previously treated patients with advanced liposarcoma or leiomyosarcoma: a randomised, open-label, multicentre, phase 3 trial [published online February 10, 2016]. *Lancet.* 2016;387(10028):1629-1637. doi:10.1016/S0140-6736(15)01283-0. **4.** Tseng WW, Somaiah N, Lazar AJ, Lev DC, Pollock RE. Novel systemic therapies in advanced liposarcoma: a review of recent clinical trial results. *Cancers (Basel).* 2013;5(2):529-549.

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