

WE STAND
UNITED
FOR
BLOOD CANCER
AWARENESS
MONTH



Conference call to discuss FDA
approval of COPIKTRA™ (duvelisib)
September 24, 2018

Forward Looking Statements

This presentation includes forward-looking statements about, among other things, Verastem Oncology's products and product candidates, including anticipated regulatory submissions, approvals, performance and potential benefits of Verastem Oncology products and product candidates, that are subject to substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements.

Additional information regarding these factors can be found in Verastem's Annual Report on Form 10-K for the fiscal year ended December 31, 2017 and in our subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors that May Affect Future Results", as well as in our subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission (SEC) and available at www.sec.gov and www.verastem.com.

The forward-looking statements in this presentation speak only as of the original date of this presentation, and we undertake no obligation to update or revise any of these statements.

Introduction

Robert Forrester
Chief Executive Officer



Copiktra™

(duvelisib) 15mg | 25mg capsules

The first approved dual inhibitor of PI3K delta and gamma is

NOW AVAILABLE

COPIKTRA is a kinase inhibitor indicated for the treatment of adult patients with:

- Relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies.
- Relapsed or refractory follicular lymphoma (FL) after at least two prior systemic therapies.

This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Full Prescribing Information, including BOXED WARNING and Medication Guide, is available at www.COPIKTRA.com

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Indication

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- Relapsed or refractory follicular lymphoma (FL) after at least two prior systemic therapies.

This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Dosing & Administration

25 mg orally, twice daily. Modify dosage for toxicity.

Selected Important Safety Information

WARNING: FATAL AND SERIOUS TOXICITIES: INFECTIONS, DIARRHEA OR COLITIS, CUTANEOUS REACTIONS, and PNEUMONITIS

- Fatal and/or serious infections occurred in 31% of COPIKTRA-treated patients. Monitor for signs and symptoms of infection. Withhold COPIKTRA if infection is suspected.
- Fatal and/or serious diarrhea or colitis occurred in 18% of COPIKTRA-treated patients. Monitor for the development of severe diarrhea or colitis. Withhold COPIKTRA.
- Fatal and/or serious cutaneous reactions occurred in 5% of COPIKTRA-treated patients. Withhold COPIKTRA.
- Fatal and/or serious pneumonitis occurred in 5% of COPIKTRA-treated patients. Monitor for pulmonary symptoms and interstitial infiltrates. Withhold COPIKTRA.

Warnings and Precautions

- Hepatotoxicity: Monitor hepatic function.
- Neutropenia: Monitor blood counts.
- Embryo-Fetal toxicity: COPIKTRA can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.

Contraindications: None.

Most common adverse reactions ($\geq 20\%$): Diarrhea or colitis, neutropenia, rash, fatigue, pyrexia, cough, nausea, upper respiratory infection, pneumonia, musculoskeletal pain, and anemia.

Source: Copiktra USPI, 2018

COPIKTRA™ (duvelisib) capsules

Dan Paterson
Chief Operating Officer

Duvelisib clinical development as a monotherapy

7

SCIENTIFIC HYPOTHESIS

Unique dual PI3K inhibition results in monotherapy efficacy with a consistent safety profile

UNMET NEED

For patients with chronic indolent lymphoma progressing on treatment, additional therapy options are needed

δ & γ

(delta) (gamma)

Duvelisib targets both malignant B cells and their supportive tumor microenvironment



1 capsule, twice a day

Duvelisib offers oral monotherapy dosing for at-home disease management

DEVELOPMENT RATIONALE

Duvelisib monotherapy may **expand** treatment options for patients living with chronic indolent lymphomas

Pivotal trials for duvelisib monotherapy in indolent NHL



A phase 2 study of duvelisib monotherapy in double refractory* iNHL populations

**Refractory to both rituximab and a chemotherapy or radioimmunotherapy regimen*

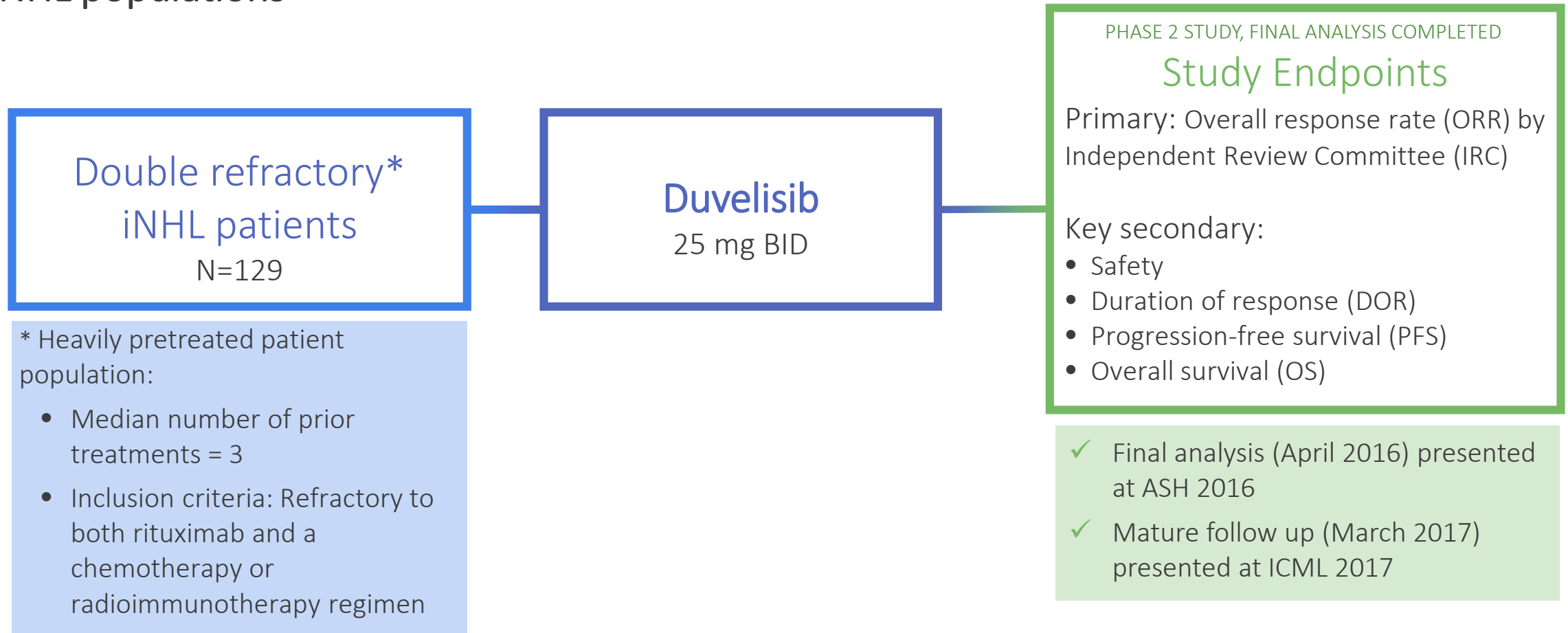


A phase 3 randomized study of duvelisib monotherapy in relapsed/refractory CLL/SLL

Randomized vs. ofatumumab, with optional cross-over following progression

DYNAMO™

A phase 2 study of duvelisib monotherapy in double refractory iNHL populations



Phase 2 study results

Met primary endpoint of Overall Response Rate (ORR) assessed by IRC

Patient population:

Patients with iNHL that is refractory to both rituximab and a chemotherapy or radioimmunotherapy regimen

Primary endpoint:

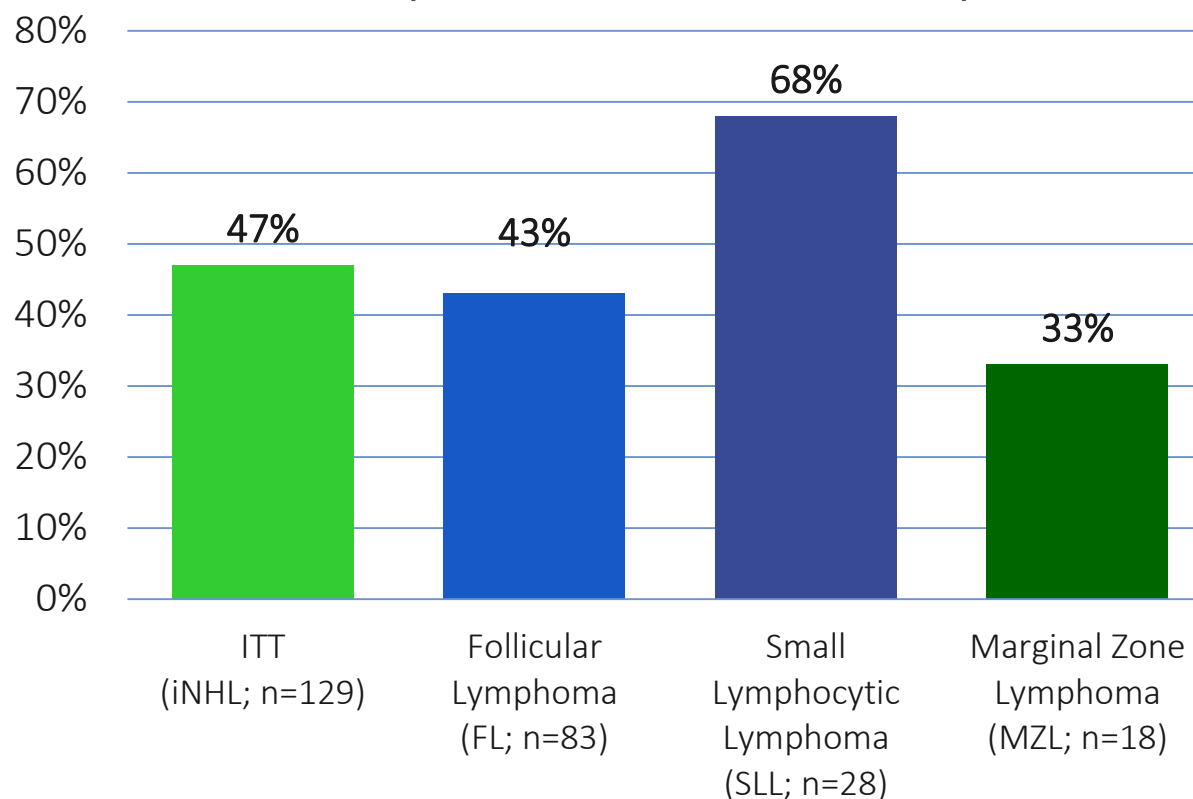
- ORR by IRC at per-protocol final analysis: (p=0.0001)

Secondary endpoint:

- Median DOR: 10 months

Source: Zinzani et al., ICML 2017

ORR per IRC at mature follow up



COPIKTRA is approved for the treatment of adult patients with relapsed or refractory follicular lymphoma after at least two prior systemic therapies. Accelerated approval was granted in this indication based on overall response rate (ORR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

For full prescribing and safety information, please refer to the Package Insert and Important Safety Information available at www.COPIKTRA.com.

Data supporting FL accelerated approval

Overall Response Rate (ORR) assessed by IRC

Efficacy in Patients with Relapsed or Refractory FL

Endpoint	FL N = 83
ORR, n (%) ^a	35 (42%)
95% CI	(31, 54)
CR, n (%)	1 (1%)
PR, n (%)	34 (41%)
Duration of response	
Range, months	0.0 ⁺ to 41.9 ⁺
Patients maintaining response at 6 months, n/N (%)	15/35 (43%)
Patients maintaining response at 12 months, n/N (%)	6/35 (17%)

Abbreviations: CI = confidence interval; CR = complete response; IRC = Independent Review Committee; ORR = overall response rate; PR = partial response

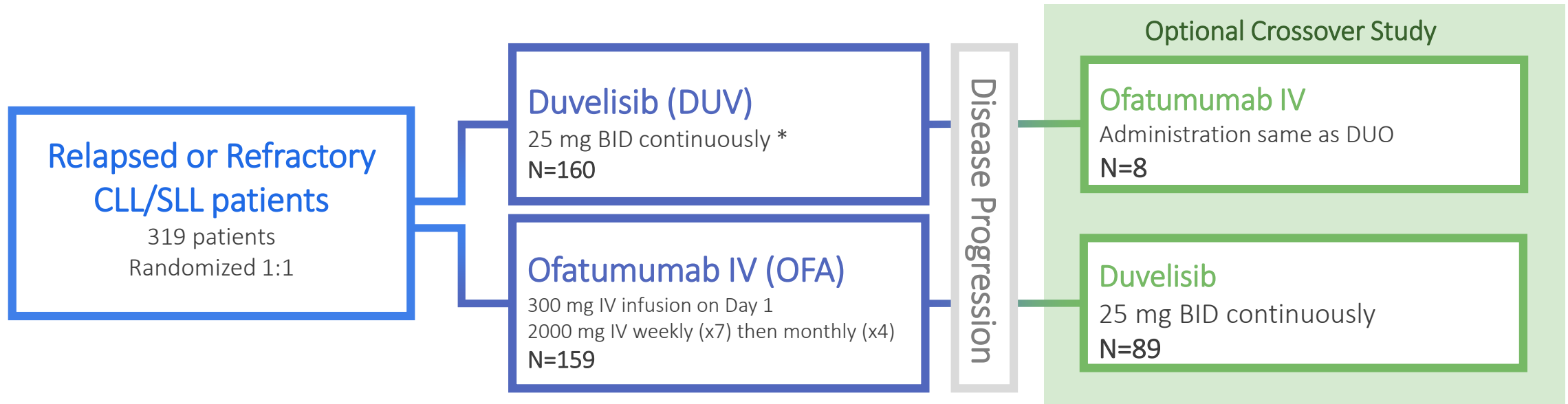
^a Per IRC according to Revised International Working Group criteria

⁺ Denotes censored observation

Source: Copiktra USPI, 2018

COPIKTRA is approved for the treatment of adult patients with relapsed or refractory follicular lymphoma after at least two prior systemic therapies. Accelerated approval was granted in this indication based on overall response rate (ORR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

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Median prior lines of therapy: 2

Endpoints

- PFS (primary)
- ORR, DOR, OS (secondary)
- Safety (AEs and lab abnormalities)

Response per modified iwCLL/IWG Criteria **

- Assessed by independent review committee (IRC)
- Cycle 3 (C3), C5, C7, C11, C15, C19, every 6 months thereafter
- CT scan, CBC, disease related symptoms, BM biopsy ***
- Survival assessment every 6 months

* Patients may have stopped treatment at C18 for CR/PR >3 months at discretion of Investigator

** Lymphocytosis not considered disease progression; PR = 2 Group A and 1 Group B Criteria

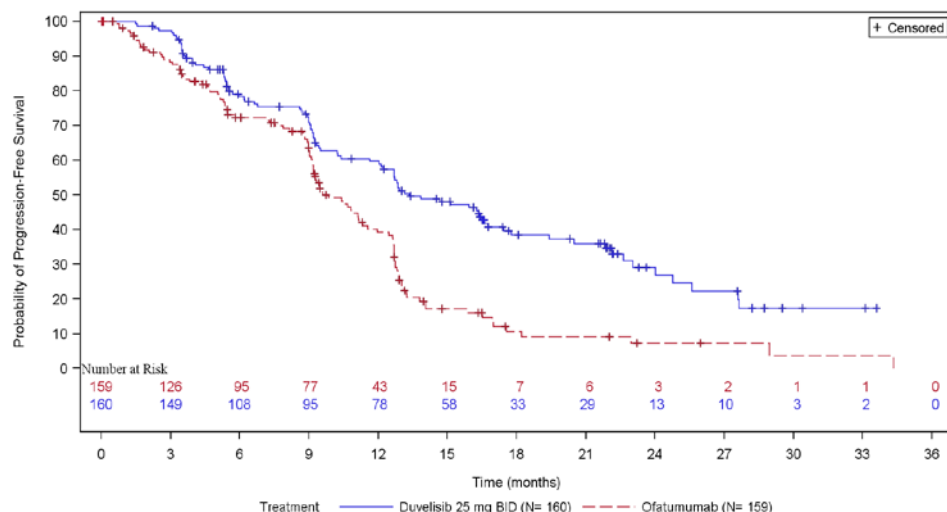
*** Required for confirmation of CR/CRi



Phase 3 study results

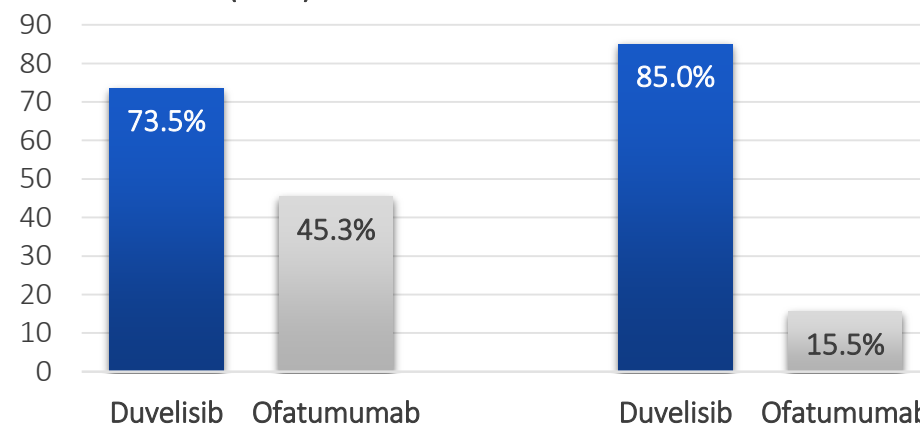
Met primary endpoint of PFS by IRC, with significant improvements in ORR and LNRR

Progression Free Survival (PFS) by IRC



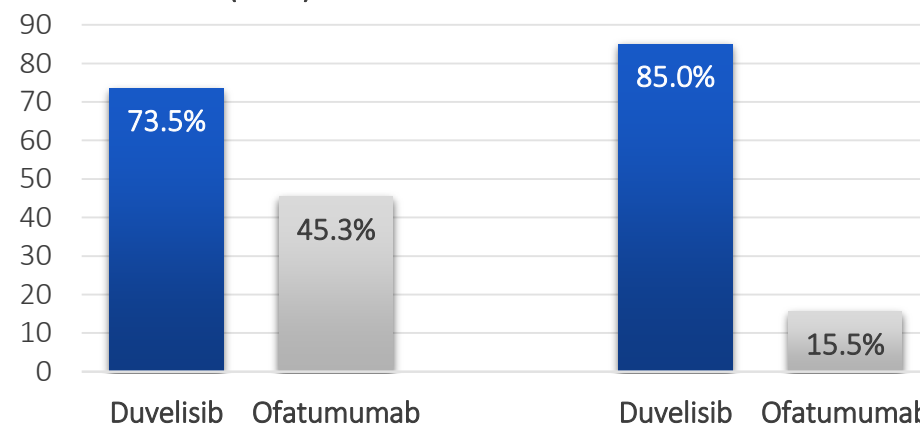
	Duvelisib	Ofatumumab
Median PFS (Months)	13.3	9.9
95% CI	12.1, 16.8	9.2, 11.3
Hazard ratio	0.52	
p-value	< 0.0001	

Overall Response Rate (ORR)



	Duvelisib	Ofatumumab
CR	0.6%	0.6%
PRwL	0.6%	0
PR	72.5%	44.7%
p-value	< 0.0001	

Lymph Node Response Rate



COPIKTRA is approved for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.

For full prescribing and safety information, please refer to the Package Insert and Important Safety Information available at www.COPIKTRA.com.

Source: Flinn et al., ASH 2017

Efficacy supporting full approval in CLL/SLL

Greater benefit/risk for patients receiving two or more prior therapies

Efficacy in CLL or SLL After at Least Two Prior Therapies

Outcome per IRC	COPIKTRA N = 95	Ofatumumab N = 101
PFS		
Number of events, n (%)	55 (58%)	70 (69%)
Progressive disease	44	62
Death	11	8
Median PFS (SE), months ^a	16.4 (2.1)	9.1 (0.5)
Hazard Ratio (SE), ^b COPIKTRA/ofatumumab	0.40 (0.2)	
Response rate		
ORR n (%) ^c	74 (78%)	39 (39%)
CR	0 (0%)	0 (0%)
PR	74 (78%)	39 (39%)
Difference in ORR, % (SE)	39% (6.4)	

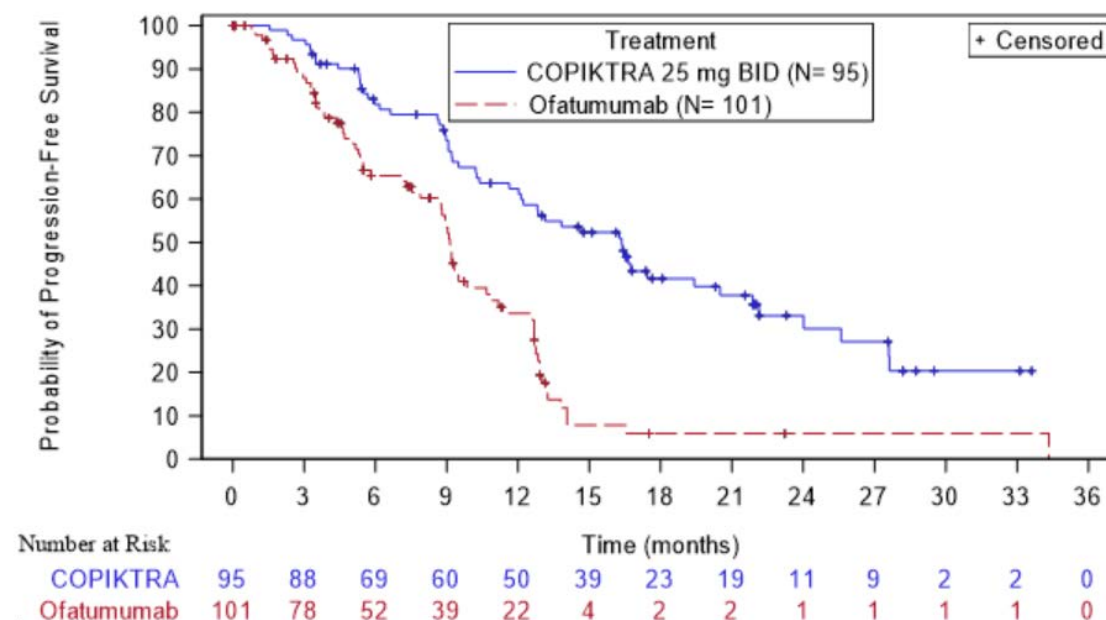
Abbreviations: CI = confidence interval; CR = complete response; IRC = Independent Review Committee; PFS = progression-free survival; PR = partial response; SE = standard error

^a Kaplan-Meier estimate

^b Standard Error of ln(hazard ratio) = 0.2

^c IWCLL or revised IWG response criteria, with modification for treatment-related lymphocytosis

Kaplan-Meier Curve of PFS per IRC In Patients with at Least 2 Prior Therapies



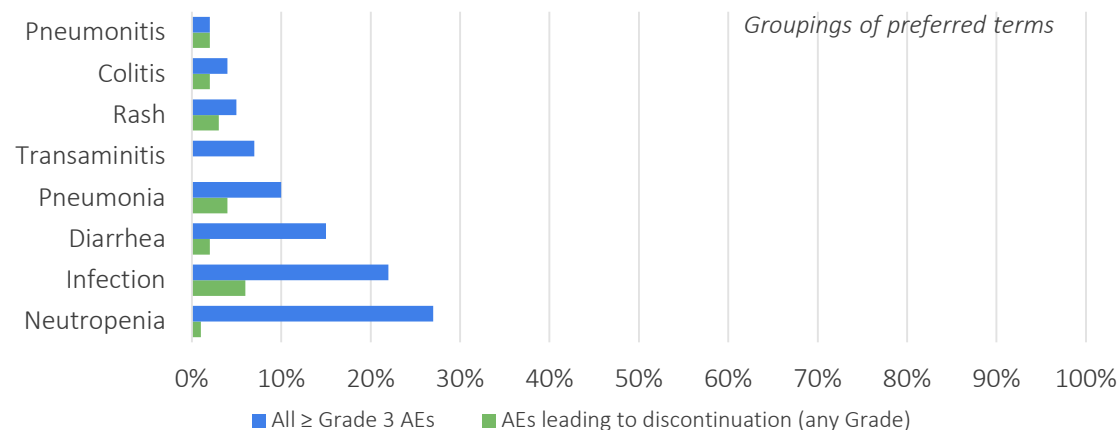
Source: Copiktra USPI, 2018

COPIKTRA is approved for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.

For full prescribing and safety information, please refer to the Package Insert and Important Safety Information available at www.COPIKTRA.com.

Consistent safety and tolerability profile across B-cell malignancies

15

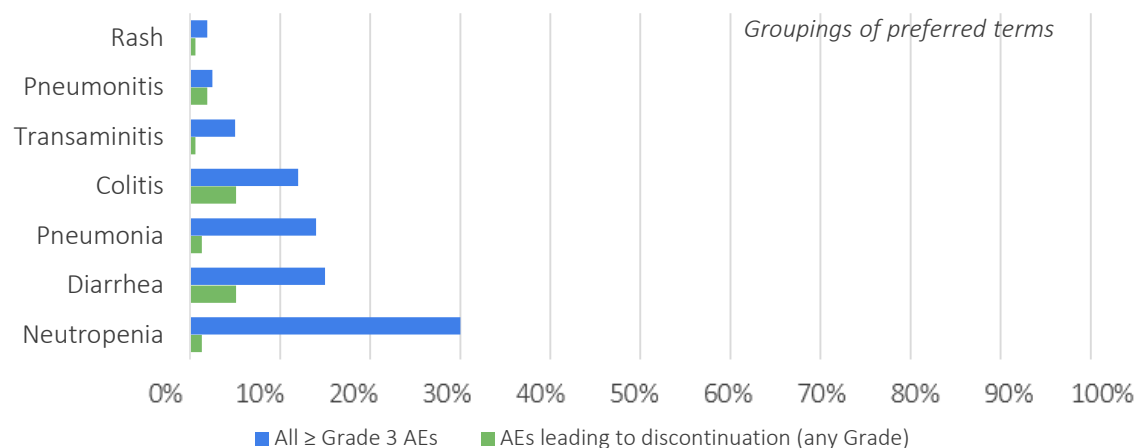


- Serious opportunistic infections < 4%: PCP (unconfirmed) (n=1); CMV (n=2); fungal pneumonia (n=2)

- Deaths attributed to treatment (n=6)*

* colitis (n=1); toxic epidermal necrolysis/sepsis syndrome (n=1); drug reaction/eosinophilia/systemic symptoms (n=1); pneumonitis/pneumonia (n=1); viral infection (n=1); septic shock (n=1)

Source: Zinzani et al., ICML 2017



- Severe opportunistic infections (6%): bronchopulmonary aspergillosis (n=4), fungal infection (n=2), Pneumocystis jirovecii pneumonia (n=2)*, and cytomegalovirus colitis (n=1)

- No severe herpes zoster infections

- Deaths attributed to treatment (n=4)**

* Neither patient on prophylaxis at the time of the event

** general health deterioration (n=1); pneumonia staphylococcal (n=2); sepsis (n=1)

Source: Flinn et al., ASH 2017

Pooled analysis of safety supporting approval

442 patients with previously treated hematologic malignancies

Most Common Adverse Reactions (≥ 10% Grade ≥ 3 or ≥ 20% Any Grade) in Patients with B-cell Malignancies Receiving COPIKTRA

Adverse Reactions	COPIKTRA 25 mg BID (N = 442)	
	Grade ≥ 3 n (%)	Any Grade n (%)
Neutropenia †	132 (30%)	151 (34%)
Diarrhea or colitis † ^a	101 (23%)	222 (50%)
Pneumonia † ^b	67 (15%)	91 (21%)
Anemia †	48 (11%)	90 (20%)
Rash † ^c	41 (9%)	136 (31%)
Fatigue †	22 (5%)	126 (29%)
Pyrexia	7 (2%)	115 (26%)
Musculoskeletal pain †	6 (1%)	90 (20%)
Nausea †	4 (<1%)	104 (24%)
Cough †	2 (<1%)	111 (25%)
Upper respiratory tract infection †	2 (<1%)	94 (21%)

† Grouped term for reactions with multiple preferred terms

^a Diarrhea or colitis includes the preferred terms: colitis, enterocolitis, colitis microscopic, colitis ulcerative, diarrhea, diarrhea hemorrhagic

^b Pneumonia includes the preferred terms: All preferred terms containing "pneumonia" except for "pneumonia aspiration"; bronchopneumonia, bronchopulmonary aspergillosis

^c Rash includes the preferred terms: dermatitis (including allergic, exfoliative, perivascular), erythema (including multiforme), rash (including exfoliative, erythematous, follicular, generalized, macular & papular, pruritic, pustular), toxic epidermal necrolysis and toxic skin eruption, drug reaction with eosinophilia and systemic symptoms, drug eruption, Stevens-Johnson syndrome

Serious adverse reactions were reported in 289 patients (65%). The most frequent serious adverse reactions that occurred were:

- infection (31%) †
- diarrhea or colitis (18%) †
- pneumonia (17%) †
- rash (5%) †
- pneumonitis (5%) †

For full prescribing and safety information, please refer to the Package Insert and Important Safety Information available at www.COPIKTRA.com.

Source: Copiktra USPI, 2018



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Contraindications: None.

Most common adverse reactions ($\geq 20\%$): Diarrhea or colitis, neutropenia, rash, fatigue, pyrexia, cough, nausea, upper respiratory infection, pneumonia, musculoskeletal pain, and anemia.

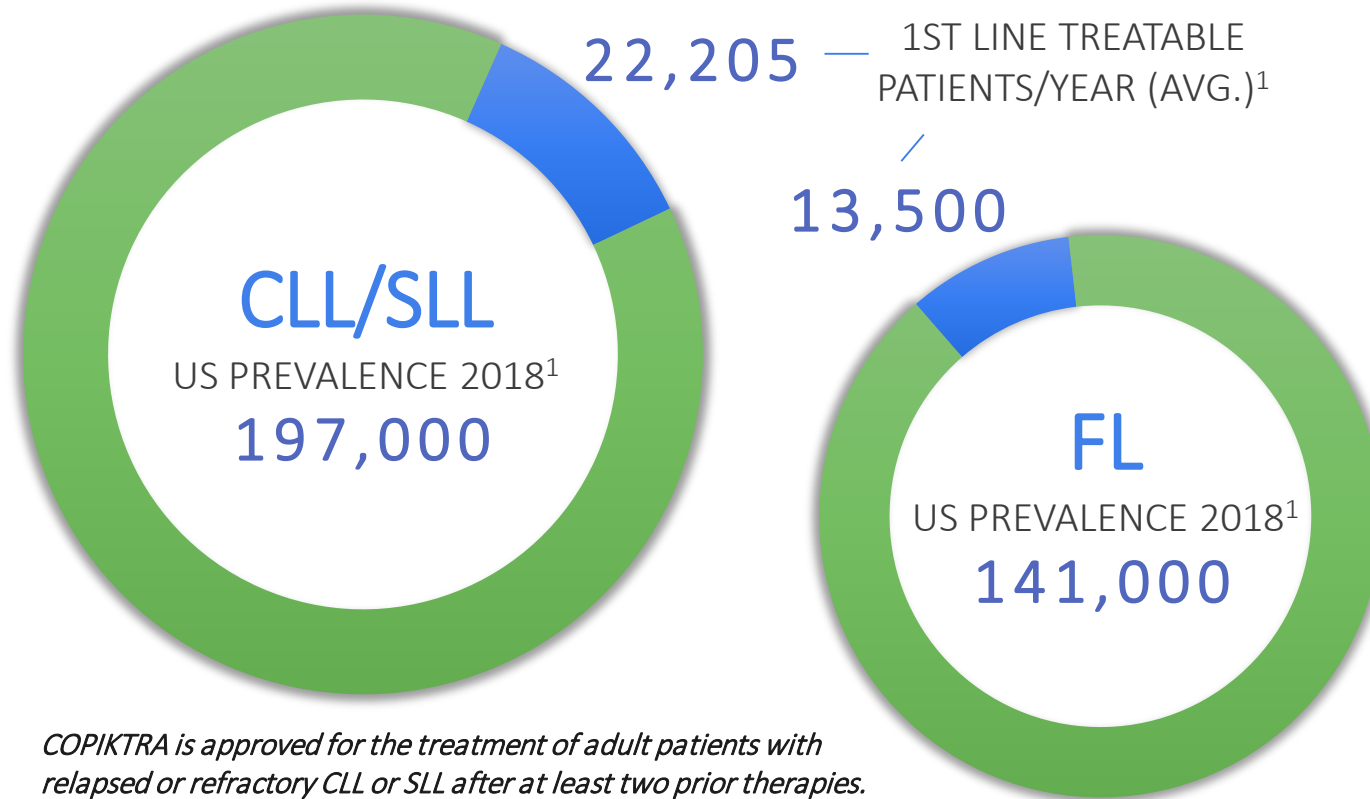
Source: Copiktra USPI, 2018

Commercial launch

Joe Lobacki

Chief Commercial Officer

Additional therapy options are needed for chronic iNHL patients



COPIKTRA is approved for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.

COPIKTRA is approved for the treatment of adult patients with relapsed or refractory follicular lymphoma after at least two prior systemic therapies. Accelerated approval was granted in this indication based on overall response rate (ORR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Increasing Elderly At-Risk Patient Population

65-75

AGE AT
DIAGNOSIS²

AGING BABY BOOMER
POPULATION

INCREASED DIAGNOSES

Additional Therapy Options Needed for Chronic Disease Control

MEDIAN OS

10+ YEARS³

NEED FOR MORE LINES
OF THERAPY

INCREASED DEMAND FOR
ORAL TARGETED THERAPIES

Sources: 1. Decision Resources, 2016-2018 annual estimates; 2. SEER, FL and CLL statistics; 3. NHI, NHL and CLL PDQ

The COPIKTRA™ opportunity in relapsed or refractory FL after two prior systemic therapies

COPIKTRA provides a targeted therapy option after chemo-immunotherapy

20

80%

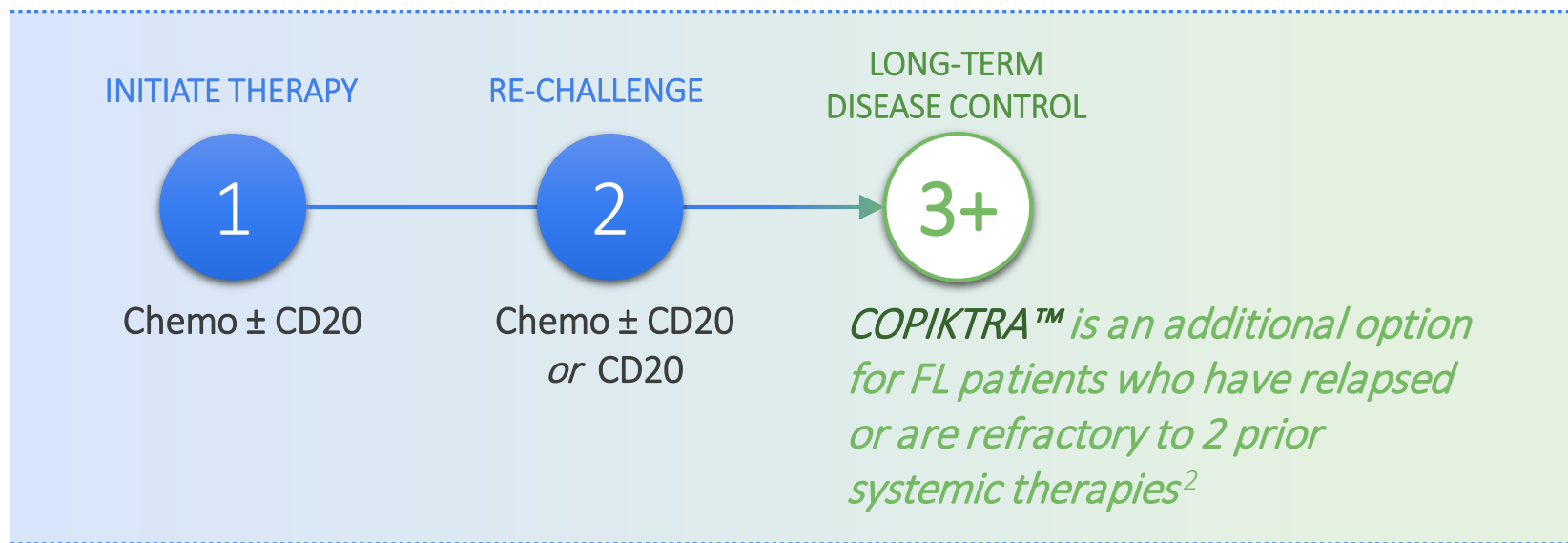
receive chemo or anti-CD20 again in 2nd line therapy

>80% of 2nd line treated FL patients are still re-challenged with a chemotherapy or anti-CD20 based regimen

Oral targeted therapies provide new treatment options

2ND LINE¹

For FOLLICULAR LYMPHOMA patients considering their next therapy ● ● ○



Sources: 1. ATU 2018, Verastem Oncology; 2. Copiktra USPI, Accelerated Approval

COPIKTRA is approved for the treatment of adult patients with relapsed or refractory follicular lymphoma after at least two prior systemic therapies. Accelerated approval was granted in this indication based on overall response rate (ORR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

For full prescribing and safety information, please refer to the Package Insert and Important Safety Information available at www.COPIKTRA.com.

The COPIKTRA™ opportunity in relapsed or refractory CLL/SLL after two prior therapies

COPIKTRA expands oral monotherapy opportunities

70%

initiate therapy with chemo or anti-CD20

Preference for oral targeted therapies is steadily growing:

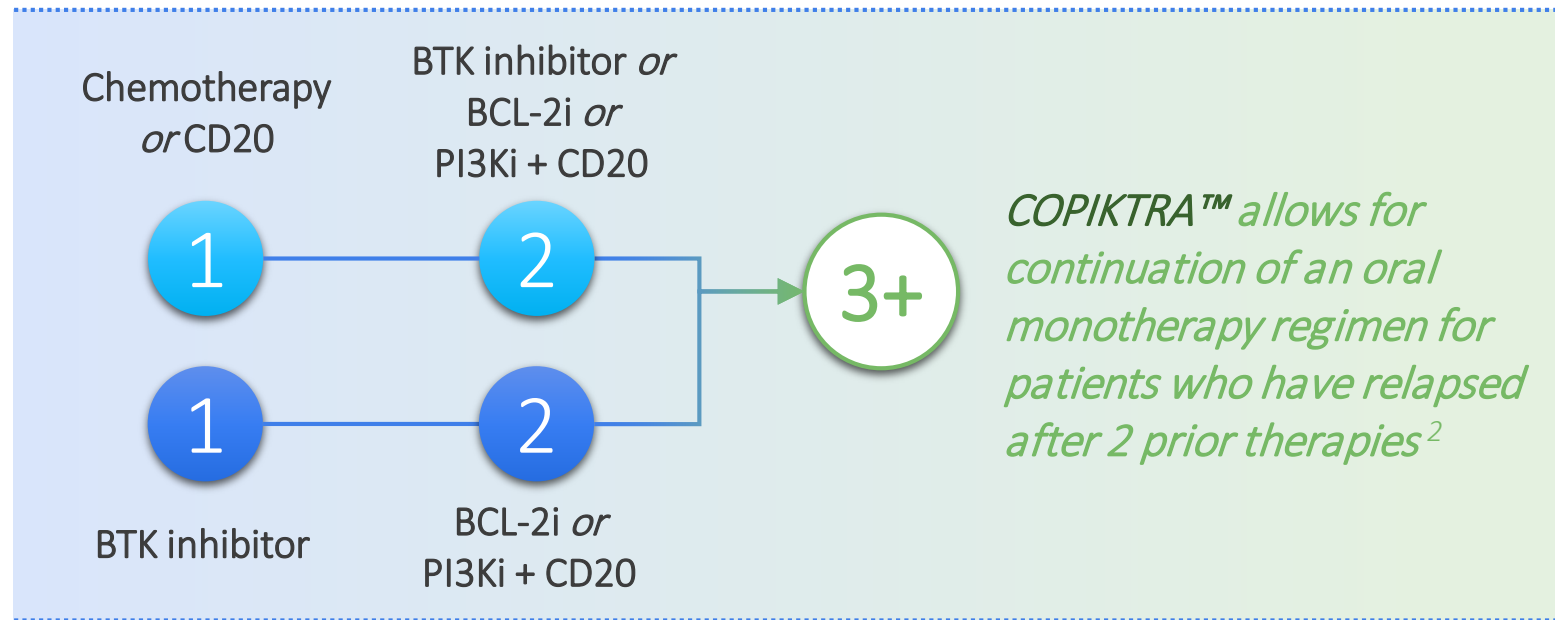
30% of patients now initiate treatment on a BTK inhibitor, instead of a chemo- or anti-CD20 based regimen

30%

start with targeted therapy

1st LINE¹

For CHRONIC LYMPHOCYTIC LEUKEMIA / SMALL LYMPHOCYTIC LYMPHOMA patients considering their next therapy ● ● ○



Sources: 1. ATU 2018, Verastem Oncology; 2. Copiktra USPI, Full Approval

COPIKTRA is approved for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.

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Making COPIKTRA available



*"How can we better
Care Differently for you
today?"*

*Experienced senior commercial and medical affairs leadership, with a focused field force providing **One Voice** to the customer*

- Senior leadership has an average of 24+ years industry experience and participation in over 30 drug launches
- 50 person Oncology sales team
- Dedicated Medical Affairs & Patient Advocacy teams
- Oncology nurse advocates providing access support and education
- Experienced supporting team in Marketing, Patient Services, Reimbursement, and Market Access

*Targeting key
HCPs and
reimbursement
coverage*

Specialty Pharmacy Providers

- 92% coverage of all US cases ■



Specialty Distributors

- 100% coverage ■



All logos and trademarks are the property of their respective owners.

For full prescribing and safety information, please refer to the Package Insert and Important Safety Information available at www.COPIKTRA.com.

COPIKTRA value



CLINICAL OUTCOMES AND NEED

COPIKTRA is an effective oral monotherapy regimen with a consistent safety profile

Copiktra has been granted full approval for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.

*Copiktra has been granted accelerated approval in adult patients with relapsed or refractory follicular lymphoma after two prior systemic therapies. **Safety and efficacy in this patient population have not been confirmed.** Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.*



PATIENT BENEFIT

COPIKTRA patients can maintain flexibility in daily life with at-home dosing



HEALTH ECONOMICS

COPIKTRA offers monotherapy administration, with no required hospitalization or infusion



- Monthly list price: \$11,800
- Price may vary per individual insurance coverage including government programs

For full prescribing and safety information, please refer to the Package Insert and Important Safety Information available at www.COPIKTRA.com.

Verastem *Cares*. Go beyond the expected



ACCESS *Cancer is hard enough – let's keep it simple.*

For the majority of patients and their healthcare providers, **stay with the system** that already works for you



ASSISTANCE *Patients prescribed COPIKTRA should have access to therapy.*

- **Bridge Program** provides product for eligible patients with delays in reimbursement coverage over 5 days
- **Prescription Assistance Program (PAP)** provides therapy for eligible patients in need

SUPPORT *Patients should always have somewhere to turn.*

Oncology nurse advocates are here to listen and assist

COMMUNITY *Patients should never feel alone.*

Let us make connections to patients and caregivers like you through external cancer support organizations

All logos and trademarks are the property of their respective owners.

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Future Potential of COPIKTRA

TODAY:

ANCHOR

Approved in the US as monotherapy for R/R FL and CLL/SLL after 2 prior lines¹

FL: 13,000 incidence,
141,000 prevalence²
CLL: 23,000 incidence,
197,000 prevalence²

BROADEN REACH

Expand in FL and CLL/SLL
Expand into PTCL[†]

BOLD STEPS

Combinations with I-O and SOC in aggressive NHL subtypes
DLBCL, MCL, Richter's, Transformed FL[†]

MAXIMIZE POTENTIAL

Combinations with novel agents and CAR-T
NHL, Myeloma, Solid Tumors[†]

STEP 4

STEP 3

STEP 2

STEP 1

Sources:

1. Copiktra USPI, 2018 – Accelerated Approval in FL, Full approval in CLL/SLL;
2. Decision Resources, US 2018²

IP
Composition of Matter: 2030

[†] COPIKTRA is not indicated for use in the treatment of these indications, and the safety and efficacy of COPIKTRA in these indications has not been established. Any such use is investigational only. COPIKTRA has been granted full approval for the treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies.

COPIKTRA is approved for the treatment of adult patients with relapsed or refractory follicular lymphoma after at least two prior systemic therapies. Accelerated approval was granted in this indication based on overall response rate (ORR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

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The first approved dual inhibitor of PI3K delta and gamma is

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INDICATIONS AND USAGE

COPIKTRA™ (duvelisib) is indicated for:

The treatment of adult patients with relapsed or refractory CLL or SLL after at least two prior therapies; and

The treatment of adult patients with relapsed or refractory FL after at least two prior systemic therapies.

This indication is approved under accelerated approval based on overall response rate (ORR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

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- Fatal and/or serious pneumonitis occurred in 5% of COPIKTRA-treated patients. Monitor for pulmonary symptoms and interstitial infiltrates. Withhold COPIKTRA.

WARNINGS AND PRECAUTIONS

Infections: Serious, including fatal (18/442; 4%), infections occurred in 31% of patients receiving COPIKTRA 25 mg BID (N=442). The most common serious infections were pneumonia, sepsis, and lower respiratory infections. Median time to onset of any grade infection was 3 months (range: 1 day to 32 months), with 75% of cases occurring within 6 months. Treat infections prior to initiation of COPIKTRA. Advise patients to report new or worsening signs and symptoms of infection. For grade 3 or higher infection, withhold COPIKTRA until infection is resolved. Resume COPIKTRA at the same or reduced dose. Serious, including fatal, *Pneumocystis jirovecii* pneumonia (PJP) occurred in 1% of patients taking COPIKTRA. Provide prophylaxis for PJP during treatment with COPIKTRA and following completion of treatment with COPIKTRA until the absolute CD4+ T cell count is greater than 200 cells/μL. Withhold COPIKTRA in patients with suspected PJP of any grade, and permanently discontinue if PJP is confirmed. Cytomegalovirus (CMV) reactivation/infection occurred in 1% of patients taking COPIKTRA. Consider prophylactic antivirals during COPIKTRA treatment to prevent CMV infection including CMV reactivation. For clinical CMV infection or viremia, withhold COPIKTRA until infection or viremia resolves. If COPIKTRA is resumed, administer the same or reduced dose and monitor patients for CMV reactivation by PCR or antigen test at least monthly.

Diarrhea or Colitis: Serious, including fatal (1/442; <1%), diarrhea or colitis occurred in 18% of patients receiving COPIKTRA 25 mg BID (N=442). Median time to onset of any grade diarrhea or colitis was 4 months (range: 1 day to 33 months), with 75% of cases occurring by 8 months. The median event duration was 0.5 months (range: 1 day to 29 months; 75th percentile: 1 month). Advise patients to report any new or worsening diarrhea. For patients presenting with mild or moderate diarrhea (Grade 1-2) (i.e., up to 6 stools per day over baseline) or asymptomatic (Grade 1) colitis, initiate supportive care with antidiarrheal agents, continue COPIKTRA at the current dose, and monitor the patient at least weekly until the event resolves. If the diarrhea is unresponsive to antidiarrheal therapy, withhold COPIKTRA and initiate supportive therapy with enteric acting steroids (e.g., budesonide). Monitor the patient at least weekly. Upon resolution of the diarrhea, consider restarting COPIKTRA at a reduced dose. For patients presenting with abdominal pain, stool with mucus or blood, change in bowel habits, peritoneal signs, or with severe diarrhea (Grade 3) (i.e., > 6 stools per day over baseline), withhold COPIKTRA and initiate supportive therapy with enteric acting steroids (e.g., budesonide) or systemic steroids. A diagnostic work-up to determine etiology, including colonoscopy, should be performed. Monitor at least weekly. Upon resolution of the diarrhea or colitis, restart COPIKTRA at a reduced dose. For recurrent Grade 3 diarrhea or recurrent colitis of any grade, discontinue COPIKTRA. Discontinue COPIKTRA for life-threatening diarrhea or colitis.

IMPORTANT SAFETY INFORMATION (continued)

Cutaneous Reactions: Serious, including fatal (2/442; <1%), cutaneous reactions occurred in 5% of patients receiving COPIKTRA 25 mg BID (N= 442). Fatal cases included drug reaction with eosinophilia and systemic symptoms (DRESS) and toxic epidermal necrolysis (TEN). Median time to onset of any grade cutaneous reaction was 3 months (range: 1 day to 29 months, 75th percentile: 6 months) with a median event duration of 1 month (range: 1 day to 37 months, 75th percentile: 2 months). Presenting features for the serious events were primarily described as pruritic, erythematous, or maculo-papular. Less common presenting features include exanthem, desquamation, erythroderma, skin exfoliation, keratinocyte necrosis, and papular rash. Advise patients to report new or worsening cutaneous reactions. Review all concomitant medications and discontinue any medications potentially contributing to the event. For patients presenting with mild or moderate (Grade 1-2) cutaneous reactions, continue COPIKTRA at the current dose, initiate supportive care with emollients, antihistamines (for pruritus), or topical steroids, and monitor the patient closely. Withhold COPIKTRA for severe (Grade 3) cutaneous reaction until resolution. Initiate supportive care with steroids (topical or systemic) or antihistamines (for pruritus). Monitor at least weekly until resolved. Upon resolution of the event, restart COPIKTRA at a reduced dose. Discontinue COPIKTRA if severe cutaneous reaction does not improve, worsens, or recurs. For life-threatening cutaneous reactions, discontinue COPIKTRA. In patients with SJS, TEN, or DRESS of any grade, discontinue COPIKTRA.

Pneumonitis: Serious, including fatal (1/442; <1%), pneumonitis without an apparent infectious cause occurred in 5% of patients receiving COPIKTRA 25 mg BID (N=442). Median time to onset of any grade pneumonitis was 4 months (range: 9 days to 27 months), with 75% of cases occurring within 9 months. The median event duration was 1 month, with 75% of cases resolving by 2 months. Withhold COPIKTRA in patients with new or progressive pulmonary signs and symptoms such as cough, dyspnea, hypoxia, interstitial infiltrates on a radiologic exam, or a decline by more than 5% in oxygen saturation, and evaluate for etiology. If the pneumonitis is infectious, patients may be restarted on COPIKTRA at the previous dose once the infection, pulmonary signs and symptoms resolve. For moderate non-infectious pneumonitis (Grade 2), treat with systemic corticosteroids and resume COPIKTRA at a reduced dose upon resolution. If non-infectious pneumonitis recurs or does not respond to steroid therapy, discontinue COPIKTRA. For severe or life-threatening non-infectious pneumonitis, discontinue COPIKTRA and treat with systemic steroids.

Hepatotoxicity: Grade 3 and 4 ALT and/or AST elevation developed in 8% and 2%, respectively, of patients receiving COPIKTRA 25 mg BID (N=442). Two percent of patients had both an ALT or AST > 3 X ULN and total bilirubin > 2 X ULN. Median time to onset of any grade transaminase elevation was 2 months (range: 3 days to 26 months), with a median event duration of 1 month (range: 1 day to 16 months). Monitor hepatic function during treatment with COPIKTRA. For Grade 2 ALT/AST elevation (> 3 to 5 X ULN), maintain COPIKTRA dose and monitor at least weekly until return to < 3 X ULN. For Grade 3 ALT/AST elevation (> 5 to 20 X ULN), withhold COPIKTRA and monitor at least weekly until return to < 3 X ULN. Resume COPIKTRA at the same dose (first occurrence) or at a reduced dose for subsequent occurrences. For grade 4 ALT/AST elevation (> 20 X ULN), discontinue COPIKTRA.

Neutropenia: Grade 3 or 4 neutropenia occurred in 42% of patients receiving COPIKTRA 25 mg BID (N=442), with Grade 4 neutropenia occurring in 24% of all patients. Median time to onset of grade ≥ 3 neutropenia was 2 months (range: 3 days to 31 months), with 75% of cases occurring within 4 months. Monitor neutrophil counts at least every 2 weeks for the first 2 months of COPIKTRA therapy, and at least weekly in patients with neutrophil counts < 1.0 Gi/L (Grade 3-4). Withhold COPIKTRA in patients presenting with neutrophil counts < 0.5 Gi/L (Grade 4). Monitor until ANC is > 0.5 Gi/L, then resume COPIKTRA at same dose for the first occurrence or at a reduced dose for subsequent occurrences.

Embryo-Fetal Toxicity: Based on findings in animals and its mechanism of action, COPIKTRA can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Conduct pregnancy testing before initiating COPIKTRA treatment. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment and for at least 1 month after the last dose.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS

B-cell Malignancies Summary

Fatal adverse reactions within 30 days of the last dose occurred in 8% (36/442) of patients treated with COPIKTRA 25 mg BID. Serious adverse reactions were reported in 289 patients (65%). The most frequent serious adverse reactions that occurred were infection (31%), diarrhea or colitis (18%), pneumonia (17%), rash (5%), and pneumonitis (5%). Adverse reactions resulted in treatment discontinuation in 156 patients (35%) most often due to diarrhea or colitis, infection, and rash. COPIKTRA was dose reduced in 104 patients (24%) due to adverse reactions, most often due to diarrhea or colitis and transaminase elevation. The most common adverse reactions (reported in $\geq 20\%$ of patients) were diarrhea or colitis, neutropenia, rash, fatigue, pyrexia, cough, nausea, upper respiratory infection, pneumonia, musculoskeletal pain and anemia.

CLL/SLL

Fatal adverse reactions within 30 days of the last dose occurred in 12% (19/158) of patients treated with COPIKTRA and in 4% (7/155) of patients treated with ofatumumab. Serious adverse reactions were reported in 73% (115/158) of patients treated with COPIKTRA and most often involved infection (38%; 60/158) and diarrhea or colitis (23%; 36/158). COPIKTRA was discontinued in 57 patients (36%), most often due to diarrhea or colitis, infection, and rash. COPIKTRA was dose reduced in 46 patients (29%) due to adverse reactions, most often due to diarrhea or colitis and rash. The most common adverse reactions with COPIKTRA (reported in $\geq 20\%$ of patients) were diarrhea or colitis, neutropenia, pyrexia, upper respiratory tract infection, pneumonia, rash, fatigue, nausea, anemia and cough.

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Serious adverse reactions were reported in 58% of patients and most often involved diarrhea or colitis, pneumonia, renal insufficiency, rash, and sepsis. The most common adverse reactions ($\geq 20\%$ of patients) were diarrhea or colitis, nausea, fatigue, musculoskeletal pain, rash, neutropenia, cough, anemia, pyrexia, headache, mucositis, abdominal pain, vomiting, transaminase elevation, and thrombocytopenia. Adverse reactions resulted in COPIKTRA discontinuation in 29% of patients, most often due to diarrhea or colitis and rash. COPIKTRA was dose reduced in 23% due to adverse reactions, most often due to transaminase elevation, diarrhea or colitis, lipase increased and infection.

DRUG INTERACTIONS

CYP3A Inducers: Coadministration with a strong CYP3A inducer may reduce COPIKTRA efficacy. Avoid coadministration with strong CYP3A4 inducers.

CYP3A Inhibitors: Coadministration with a strong CYP3A inhibitor may increase the risk of COPIKTRA toxicities. Reduce COPIKTRA dose to 15 mg BID when coadministered with a strong CYP3A4 inhibitor.

CYP3A Substrates: Coadministration of COPIKTRA with sensitive CYP3A4 substrates may increase the risk of toxicities of these drugs. Consider reducing the dose of the sensitive CYP3A4 substrate and monitor for signs of toxicities of the coadministered sensitive CYP3A substrate.

Please see www.COPIKTRAHCP.com for full Prescribing Information, including **Boxed Warning** and Medication Guide.

To report side effects during use of COPIKTRA, contact Verastem Oncology at 1-877-7RXVSTM (1-877-779-8786) and/or the FDA at 1-800-FDA-1088 (www.fda.gov/medwatch).

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