GlobalData》
OpportunityAnalyser

ACUTE MYELOID LEUKEMIA (AML) - OPPORTUNITY ANALYSIS AND FORECASTS TO 2017

Executive Summary

AML: Key Metrics in Six Major Pharmaceutical Markets, 2012–2017	
2012 Epidemiology	
Incident Population[a]	21,798
Treated Population[a]	18,727
2012 Market Sales	
US	$108.8m
5EU	$42.2m
Total	**$151.0m**
Key events (2012–2017)	**Level of Impact**
Loss of Dacogen marketing exclusivity in the US	↓
Vosaroxin US approval for relapsed/refractory AML – 2015	↑↑
Vidaza US brand extension to 1L elderly AML – 2014	↑
Midostaurin US approval for FLT3^{+} 1L AML – 2015	↑↑
Vosaroxin EU approval for relapsed/refractory AML – 2016	↑↑
2017 Market Sales	
US	$324.4m
5EU	$106.2m
Total	**$430.7m**

Source: GlobalData.

For the purposes of this report, the six major pharmaceutical markets = US and 5EU (France, Germany, Italy, Spain, and UK).

a=Excludes APL subtype

New Entrants will Drive Strong Growth in the US and EU AML Market from 2012 to 2017

GlobalData estimates the Acute Myeloid Leukemia (AML) market in the US and 5EU (France, Germany, Italy, Spain, and UK) in 2012 to be valued at $151.0m. The market is defined as sales from branded drugs and generics commonly prescribed as induction, consolidation or salvage therapies, including cytarabine, daunorubicin, idarubicin and fludarabine. The majority of sales, $108.8m, were generated in the US, while sales in the 5EU were estimated to be $42.2m.

By 2017, the AML market is expected to grow to $430.7m at a Compound Annual Growth Rate (CAGR) of 23.3%. At the end of the forecast period, US sales will comprise a slightly larger fraction of the global market compared with 2012, with sales of $324.4m. The increase in market size, particularly in the US, will primarily be due to the launch of new therapies for AML patients with high unmet needs.
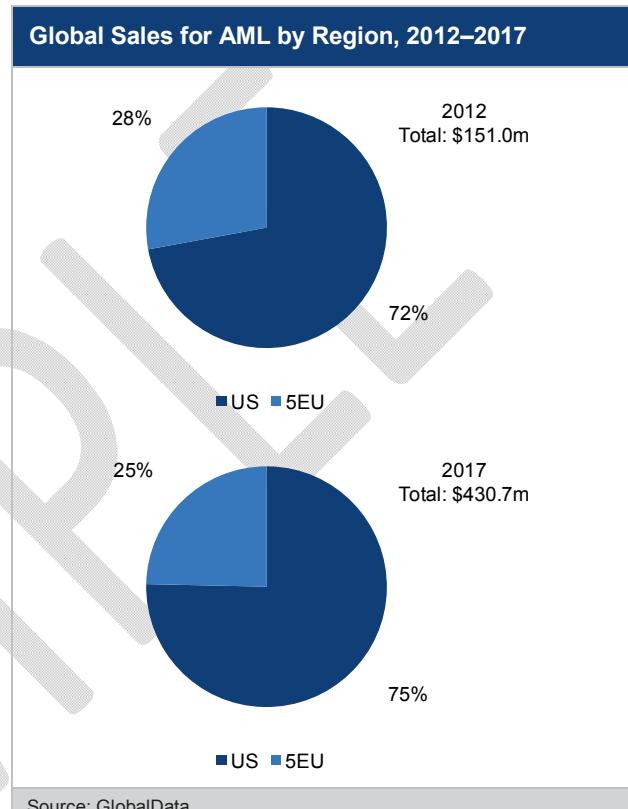
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Major drivers of the AML market in the US and 5EU will include:

- The launch of premium-priced therapies, including Sunesis' vosaroxin for relapsed/refractory AML, Novartis' midostaurin for FLT3^{+} AML, and Cyclacel's sapacitabine for newly diagnosed elderly AML.

- An increasing branded drug treatment rate, particularly among elderly patients.

- An increasing number of elderly incident cases of AML.

Barriers to the growth of the AML market in the US and 5EU will include:

- A high enrollment rate of AML patients in clinical trials in the EU.

- Pressure for cost-consciousness that will limit the reimbursement of new market entrants.

- Difficulty with developing effective therapies for AML, due to disease heterogeneity and the unclear biology of leukemogenesis.

- Unenthusiastic Key Opinion Leader (KOL) opinions regarding the efficacy of pipeline drugs.

The following figure illustrates the breakdown of sales in the global AML market, consisting of the US and 5EU.

Global Sales for AML by Region, 2012–2017

2012
Total: $151.0m

28%

72%

■US ■5EU

2017
Total: $430.7m

25%

75%

■US ■5EU

Source: GlobalData.

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R&D Strategies Target Underserved Patients and Aim to Circumvent Historical Difficulties

Although AML is a rare disease, the high levels of unmet need create ample opportunities for players with effective therapies. However, drug development has been exceedingly challenging. Drugs have showed promise in early phase, single-armed trials only to fail in larger, randomized studies. Barriers to the discovery of novel and effective therapies have included poorly designed early-phase trials, and a general lack of understanding of the biology that drives the disease.

Although the biology of AML is still poorly understood, there has been progress towards identifying actionable targets for treatment. AML patients have yet to benefit from the targeted therapies that have revolutionized the treatment of most other cancers. However, the tyrosine kinase FLT3 is currently one of the hottest targets in AML, and FLT3 inhibitors like Novartis' midostaurin and Ambit's quizartinib may prove to be valuable tools.

Players hoping to enter the space are clearly cognizant of the issues that have plagued AML drug development. Companies are designing larger, randomized Phase II trials to confirm a strong efficacy signal, before proceeding with a Phase III study. Given antecedent evidence that regulatory agencies require proof that new drugs improve patients' overall survival (OS), OS is the primary endpoint of the vast majority of ongoing Phase III trials.

Other R&D strategies discussed in this report include:

- Investigating the efficacy of pipeline drugs in combination with currently marketed chemotherapies and hypomethylating agents

- Developing industry and academic alliances

- Targeting elderly and relapsed/refractory patients

- Lifecycle management strategies involving targeting multiple AML patient segments

- The selection of appropriate clinical trial endpoints and active comparators to facilitate regulatory approval

High Unmet Needs Exist in the AML Market, Especially for Elderly and Relapsed/Refractory Patients

Adults with AML have some of the highest unmet needs of any cancer patients. Although progress has been made treating younger, favorable-risk patients, survival rates for elderly and relapsed/refractory patients are dismal. Therapies that can prolong the OS of these patients is the greatest unmet need; fulfilling this need is the surest route to regulatory approval and commercial success. However, KOLs interviewed by GlobalData highlight a number of additional unmet needs, including therapies that can eliminate minimal residual disease and induce durable complete remission (CR). While there are also environmental unmet needs that impact patients

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and physicians, including lower costs and more convenient dosing, the dire nature of AML renders these needs of lesser importance.

Pipeline Agents will Offer Incremental Improvements over Current Therapies

Like other orphan indications with great unmet needs, it is clear that effective therapies for AML can demand premium pricing. Although AML affects a relatively small number of patients, there are seven drugs in late stages of development. These drugs are primarily indicated for AML patients who respond poorly to standard chemotherapy, including newly diagnosed elderly patients (Celator's CPX-351, Cyclacel's sapacitabine, Boehringer Ingelheim's volasertib), relapsed/refractory patients (Sunesis' vosaroxin, Ambit's quizartinib) and patients with FLT3 mutations (Novartis' midostaurin, Ambit's quizartinib).

These patients' levels of unmet need are unarguably copious, which will facilitate the adoption of new drugs. GlobalData expects these drugs to demonstrate incremental OS and CR rate improvements compared with their active comparators. However, KOLs do not believe that any of these new therapies are game-changers based on the data that is currently available. Uptake will be limited, and will be higher in the US than in the 5EU.

By 2017, the AML market leader will be vosaroxin, with estimated sales of $181.3m in the US and 5EU. GlobalData does not believe that the efficacy of vosaroxin will be exceptional. However, its premium price, the sizeable population of relapsed and refractory AML patients and the absence of immediate competitions will drive higher sales from vosaroxin than any other pipeline or marketed product.

The figure below illustrates the competitive assessment of late-stage pipeline agents in AML.

Competitive Assessment of Late-Stage Pipeline Agents in AML, 2012–2017

Source: GlobalData.
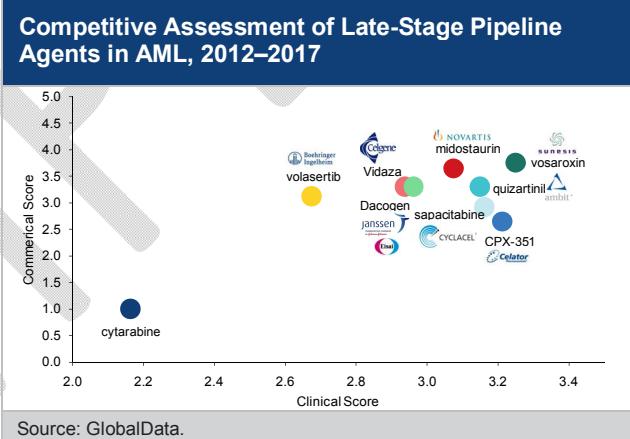
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Significant Opportunity Remains for Effective Therapies in AML

While several new agents will be launched over the forecast period, none are expected to dramatically change the treatment paradigm for AML. Drugs like Sunesis' vosaroxin, Celator's CPX-351, and Novartis' midostaurin are expected to only marginally improve the OS of various subgroups of patients. KOLs interviewed by GlobalData have an appreciation for incremental advances in the standard of care, but they agree that dramatic OS improvements are essential to improve the prognosis of AML patients.

A number of strategies exist that may help companies achieve this goal of improved OS, and capitalize on the remaining opportunity in the AML market. These include developing treatments that specifically target minimal residual disease (MRD) and combining standard chemotherapy with therapies that target driver mutations. KOLs were also positive about the concepts of employing immunotherapy as a more generalized approach to treating AML, and the development of oral maintenance therapies to help prevent relapse in patients in CR. Companies that can successfully execute one of these key strategies have the best chance of claiming the remaining market opportunity.

What Do the Physicians Think?

Although there are a number of drugs in late-stage development for AML, KOLs are largely not optimistic about imminent improvements to the standard of care.

"I think there are a lot of attempts, but nothing really in clinical practice or late-stage clinical trials that I would think, 'This is really a breakthrough'."

Germany Key Opinion Leader, June 2013

KOLs report that academic research has made progress in identifying the best courses of treatment for younger patients with core binding factor (CBF) leukemias, and for acute promyelocytic leukemia (APL). However, the majority of AML patients still are underserved by current treatment options, particularly elderly patients, high-risk patients, and those with relapsed/refractory disease.

"The major cause of death [of AML patients] is the disease…Very few people incur treatment-related mortality or die in remission. So the real problem is not less toxic therapies, the real problem is the therapies don't work."

US Key Opinion Leader, June 2013

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"Patients aged 70 today are different from patients aged 70 ten years ago. I mean, they are more active, they want treatment. So we are in front of patients who really need treatment, but we cannot give them intensive chemo because it's still too strong a treatment for them. We really need new drugs for this patient population."

EU Key Opinion Leader, June 2013

"The second [most important challenge] is relapsing patients. We cure no more than 20% of relapsing patients, and the only possibility is allogeneic stem cell transplant. But we have stem cell toxicity, and not all patients are able to receive this procedure. Another aspect is primary refractory or patients achieving CR, but who are diagnosed with high-risk disease. Because in these patients, the quality of CR is poor, and most of them experience relapse before or soon after consolidation."

EU Key Opinion Leader, May 2013

KOLs emphasize that drug developers should be looking for larger differences in CR rates and OS compared with the standard of care, not differences that barely meet the criteria statistical significance.

"I think a 20% difference [compared with the standard of care] is a big difference. If this if found to be true, a drug would certainly be licensed…"

Germany Key Opinion Leader, June 2013

"If you got a 30% CR rate [in elderly patients], that would be much better than anything that has been seen before…this is the patient group where I would think that with decitabine and low-dose cytarabine, we see a CR rate of 15% or less."

Germany Key Opinion Leader, June 2013

There is a great deal of industry interest in developing targeted therapies, particularly FLT3 inhibitors, for AML. KOLs are skeptical of these drugs' ability to control the disease as monotherapies. Instead, they believe that targeted therapies will be most effective when used in combination with standard chemotherapy.

"It is not so simple to hypothesize that beating FLT3 mutations translates into control of the disease. This is the very challenge of AML."

EU Key Opinion Leader, May 2013

"AML is a disease in which you must in some way reduce the leukemic burden…You need to reduce the leukemic burden with some kind of chemotherapy, and then refine the results [using targeted therapies]."

EU Key Opinion Leader, May 2013

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"Perhaps if we can combine different [targeted] drugs with different mechanisms of action and combine them with cytotoxic therapy – perhaps we will have better activity in these patients. But generally we are just testing one drug, and for sure we are expecting to achieve CR with one drug, and this is quite impossible."

EU Key Opinion Leader, May 2013

Although pharmaceutical companies and KOLs are interested in the development of targeted therapies, they note that the fact that designing clinical trials that enroll patients with specific molecular aberrations will be a challenge.

"When you look at the subgroups of patients who have particular abnormalities that only occur in 1%–2% of the overall AML population...Then you end up with incredibly small numbers. In a Phase III study, it is difficult to design [the trial] in such a way that you can actually come up with a statistical result at the end of the day."

UK Key Opinion Leader, June 2013

KOLs believe that carefully stratifying and randomizing early-stage trials is the key to successful pivotal studies.

"To me that is the best way to do it; to randomize as soon as we can, and get a better idea of what's going on."

US Key Opinion Leader, June 2013

"I mean, we all like to look for subgroups [within clinical data]. But to be taken seriously, a subgroup has to be corroborated on another dataset...Validation on a separate dataset is probably a good thing to do before companies put millions into doing a registration trial."

UK Key Opinion Leader, May 2013

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2.1 Catalyst

For the pharmaceuticals industry, AML has remained an elusive target for decades. The heterogeneous nature of AML coupled with a poor understanding of disease biology has complicated the drug discovery process. AML patients have yet to benefit from the targeted therapy revolution that has transformed the treatment algorithm for other cancers, and the standard of care still consists of cytarabine-based chemotherapy.

By 2017, the global AML market will welcome five new entrants. While these drugs are unlikely to completely transform the treatment algorithm, GlobalData expects them to demonstrate incremental clinical improvements in Phase III clinical studies. The increased prescription of branded therapies, particularly for newly diagnosed elderly patients and relapsed/refractory patients, will drive growth in the AML market over the forecast period.

2.3 Upcoming Related Reports

- GlobalData (2013). OpportunityAnalyzer Colorectal Cancer – Opportunity Analysis and Forecasts to 2017, August 2013.

Appendix

11.7 About GlobalData

GlobalData is a leading global provider of business intelligence in the Healthcare industry. GlobalData provides its clients with up-to-date information and analysis on the latest developments in drug research, disease analysis, and clinical research and development. Our integrated business intelligence solutions include a range of interactive online databases, analytical tools, reports and forecasts. Our analysis is supported by a 24/7 client support and analyst team.

GlobalData has offices in New York, Boston, London, India and Singapore.

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