If FDA approved oncologists could use both idelalisib and palbociclib "off label" to treat MCL.

"But there's no assurance that what you see in cell lines would be translatable into patients with the same disease," said George Canellos, M.D., a hematologic oncologist at Boston's Dana–Farber Cancer Institute. "However, looking at the molecular biology, there are a lot of consistencies between cell lines and patient-derived tissues," he added.

Chan-Kiang has already launched a clinical trial of ibrutinib plus palbociclib in MCL patients with nonmutated BTK. Meanwhile, "for an MCL patient who has failed ibrutinib and everything else, it would be fair to apply for compassionate use of idelalisib since it's already approved," said Robert Hromas, M.D., chair of the department of medicine at the University of Florida College of Medicine.

Payment would be another hurdle, Canellos added. Unless a drug company supplied the drug freely for investigational use or the treatment was part of a clinical trial, insurance companies would probably not cover it.

Chan-Kiang's study indicates another potential application for idelalisib. FDA has approved it to treat relapsed indolent chronic lymphocytic leukemia, follicular B-cell non-Hodgkin lymphoma, and relapsed small lymphocytic lymphoma. The drug is not indicated for aggressive lymphoma. Working with cell lines, Chan-Kiang and colleagues used palbociclib to turn an aggressive lymphoma into an indolent one and then kill the cells with idelalisib. Researchers are planning a multicenter clinical trial to study the drug combination in aggressive lymphoma patients; Chan-Kiang expects it to launch at the end of this year. (Researchers are also studying ibrutinib to treat indolent chronic lymphocytic leukemia.)

Dysregulation of the CDK4/CDK6 and PK13 pathways is common in human cancers, Chen-Kiang said. She anticipates that drugs that interfere with the cell cycle may be useful in treating different cancers. Moreover, "resistance will be an ongoing problem. We really need to understand how it happens and what we can do to make it better."

© Oxford University Press 2014. DOI:10.1093/jnci/dju394

Home Gardening: An Effective Cancer Therapy

By Mike Fillon

hen Joyce Sager learned she had stage I breast cancer, her oncologist recommended she start an exercise program to help her recovery. Once she got over the shock from her diagnosis, Sager joined a gym in Birmingham, Ala. In 5 years, she went only a few times. She felt guilty, but a regimented exercise program and pounding out miles on a treadmill just wasn't for her.

In summer 2013, someone approached Sager, a high school math teacher, about a program that had recently completed a pilot study. Harvest for Health is an athome gardening intervention for cancer survivors with a good prognosis and who have completed treatment. What appealed most was that a master gardener (MG) from the Alabama Cooperative Extension System would help Sager set up her garden in containers and raised beds in her own backyard.

"I always wanted to garden, but my previous attempts were miserable failures," she said.

Wendy Demark-Wahnefried, Ph.D., R.D., Webb Endowed Chair and associate director for cancer prevention and control at the University of Alabama at Birmingham Comprehensive Cancer Center, developed Harvest for Health. The program initially posed one simple question: If cancer survivors started a vegetable garden in their own yard, would they eat more vegetables? To find out, in 2011 she paired 12 adult and child cancer survivors in Jefferson County, Alabama, with MGs. This feasibility study measured how cancer survivors responded to the intervention—how it affected their diet and exercise behaviors, health-related quality of life, biomarkers of successful aging and intestinal health, and physical functioning.

Sager liked that MGs would help her decide what and how to plant, assist with problems such as irrigation and pests, and advise on when and how to harvest. Afterward, her MG would be available for consultations. She signed up and, after doing it for a year, raves about the program.

"One big plus is gardening is more interesting than a gym. Plus, watching my plants grow gives me something to look forward to every day," she said.

Demark-Wahnefried said that although many studies show links between diet or

physical activity and cancer, little is known about how gardening met these requirements. Throughout the yearlong pilot study, the survivor–MG teams planned and planted three gardens for fall, spring, and summer. They harvested and rotated each one, troubleshooting problems. Surveys collected data on diet, physical activity, and quality of life, and the study measured anthropometrics and physical function. A structured debriefing survey was part of the process also.

After 1 year, 40% of participants were eating at least one more vegetable and fruit svg/day. Demark-Wahnefried said though increasing vegetable and fruit intake was the focus, subjects also improved their exercise level. Their physical functioning improved greatly.

"Once the garden drew them outside, they were doing a lot of things around the yard, and maybe taking a walk, and other activities. As a result, the benefit that made this intervention very compelling is their improved physical function," she said.

Sixty percent of participants engaged in at least 30 min. more of physical activity/week. All improved in 3-of-4 objective measures of strength, agility, and endurance. Change scores between baseline and 1-year follow-up were as follows (median [interquartile range]) noted between baseline and 1-year follow-up)

- Hand grip test (+4.8 [3.0, 6.7] kg)
- Chair stand for 30 seconds (+3.0 [-1.0, 5.0] stands)
- Six-minute walk (+11.6 [6.1, 48.8] m)
- Get-Up-and-Go, 2.44 m (+1.0 [1.8, 0.2] seconds)

The pilot study appeared in the August 2013 *Acta Oncologica*. Forty-six cancer survivors are participating in the follow-up study. Demark-Wahnefried envisions enrolling patients with different types and stages of cancer.

Those results don't surprise Prof. Jane Maher, a National Health Service clinical leader and a consultant clinical oncologist at Mount Vernon Cancer Centre and Hillingdon Hospital in London.

"For too long, patients, friends, family, and health care professionals have believed that 'rest is always best' and that patients should take it easy during and after their cancer treatment. However, we know that that doing moderate physical activity such as gardening on a regular basis actually helps to significantly reduce the impact of side effects of cancer and its treatment, such as depression, fatigue, osteoporosis, muscle atrophy, and longer-term cardiovascular problems," she said.

Maher, also joint chief medical officer at Macmillan Cancer Support in

London, added that studies show that being active can not only help reduce side effects of grueling cancer treatment but can also reduce the risk of some cancers recurring.

"For too long, patients, friends, family, and health care professionals have believed that 'rest is always best' and that patients should take it easy during and after their cancer treatment. However,

we know that that doing moderate physical activity such as gardening on a regular basis actually helps to significantly reduce the impact of side effects of cancer and its treatment, such as depression, fatigue, osteoporosis, muscle atrophy, and longer-term cardiovascular problems."

"Breast cancer patients who undertake the recommended levels of moderate intensity physical activity (at least 150 minutes a week) could reduce their risk of dying from the disease by 30%–40%, compared to those doing less than an hour. There is no better way of putting it—physical activity is the 'wonder drug' of cancer treatment," she said.

Liz Hill Ruder, Ph.D., R.D., assistant professor and program director of the Didactic Program in Dietetics at the University of Pittsburgh, plans to develop her own Harvest for Health program. The home-based aspect of the program appealed most to her, she said.

"There are really good programs based in community gardens, but it's sometimes difficult to get cancer survivors to participate because of such things as scheduling conflicts and transportation issues. If the community garden is based at the hospital, the reminders of their disease can be an issue," she said.

Ruder, who specializes in cancer and cancer prevention, said that in addition to increased exercise and better nutrition, gardening offers cancer survivors other positive aspects.

"It can relax people, allow them an escape, reduce anxiety, and bring peace of



mind since gardening is not thought of as exercise but as a hobby—something to enjoy," she said.

Sager agrees: "I don't think of it as exercise. I putter in my garden in the

Jane Maher g

morning and after work in the evening. This has opened up another world for me. It is a labor of love."

© Oxford University Press 2014. DOI:10.1093/jnci/dju391